Dr. Amy Yasko
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Methylation Pathway Analysis

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READ IT. LEARN IT. LIVE IT.

Dr. Amy's book *Feel Good Nutrigenomics: Your Roadmap to Health* lays the basic groundwork for understanding the importance of specific SNPs in your body. For more detailed and comprehensive information on your SNPs, please consider reading Dr. Amy's book titled *Feel Good About Your SNPs* and her corresponding online presentation which is available on www.DrAmyYasko.com in the Getting Started section. You are also encouraged to visit the Getting Started section for further free resources to support your journey to better health and wellness. Please know that if you begin to feel overwhelmed, you are not alone and can join Dr. Amy's Discussion Group at www.CH3Nutrigenomics.com for additional support from others who are implementing The Yasko Protocol. As always, consult with your health care professional.

Throughout your Methylation Pathway Analysis (MPA) packet, you will find information based on the work of Dr. Amy Yasko. Each analysis is processed through a program created by Dr. Amy using her suggestions based on your genetics. Throughout the beginning pages, you will find a step by step breakdown of The Yasko Protocol. Your results begin on page 15 along with a list of supports and their associated supplement suggestions. While reviewing your results, you have the opportunity to create a Personalized Shopping List by selecting which products you would potentially like to purchase. After the last page of your results, there is a "submit" button that will create a PDF with the selected items of interest and their corresponding hyperlinks for you to reference and consult with your health care professional. At the end of this MPA, there is a General Overview of Genes section. If you would like to continue (or begin for the first time) implementing The Yasko Protocol, please consider visiting www.DrAmyYasko.com to learn more.

The information expressed in these documents does not constitute an attempt to practice medicine nor does it establish a doctor-patient relationship. This document is for informational and educational purposes only. Statements made in this document have not been evaluated by the U.S. Food & Drug Administration (FDA). The information provided is not intended to diagnose, treat, cure any disease or be used as the basis for treating a particular symptom or disease. Any products discussed or endorsed are not intended to diagnose, treat, cure any diseases or be used as the basis for treating a particular symptom or disease.

The information expressed in these documents is not meant to replace you working with a physician or health care practitioner when implementing any protocol discussed throughout these documents. Laboratory test results and comprehensive discussions or analysis of the laboratory results are intended to provide additional sources of information for you, and your physician or health care practitioner. Always seek the advice of your physician or other qualified health care practitioner with any questions you may have regarding your medical condition or as it specifically relates to implementing any protocols or suggestions discussed throughout this document.

Join Dr. Amy's Forum & Become a Member of the Discussion Group

While it may take a bit to get your arms around The Yasko Protocol, the results are truly rewarding in the long run as it is a customized program based on data. This program allows you to make choices with your health care professional based on noninvasive test data and DNA Nutrigenomic SNP data. Unlike other programs that rely on descriptions of symptoms that may have numerous causes, The Yasko Protocol adjusts with your ongoing test results to address your specific needs and imbalances over time. In comparison to other programs that use a couple of supplements that have every possible ingredient to try and make them applicable to everyone, The Yasko Protocol uses information from your personal test results, to help you choose from a range of supplements that are tailored to *your* needs.

Through her protocol, Dr. Amy's goal is to share the information you need to take your health into your own hands, creating a paradigm shift in how we deal with chronic conditions. The idea is to make you the expert on your own path to health, gathering tools so that you (with the assistance of your health care professional) can make informed health decisions and have a customized program designed just for you and your needs. Dr. Amy believes that knowledge is power and that the more you understand and the more data you have in terms of your own unique health, the better equipped you will be to make informed health decisions in the future. For this reason, Dr. Amy provides her resources at no cost so that you and your doctor can access the knowledge you need, giving you power over your own health.

A Personal Note from Dr. Amy Yasko:

Please know that the support you will receive through this Discussion Group forum is truly exceptional. This is a place for emotional support along with concrete scientific ideas. Parents can chat with each other, moderators are present to help answer questions about The Yasko Protocol, and you will see posts from me as well.

What I ask of all of our members is to put in the time to really understand the program. This will not happen overnight, it is a slow process as you immerse yourself in all of the science. Know that you will be supported, helped and guided by other veteran members of this site to make the learning process smoother and easier. This is a program that requires you to take charge of your own (or your child's) health with the guidance of your health care professional. We will share the tools and the support you need to get there, but you are going to have to put in the time and the work to get your arms around this program. No one is going to be able to do that for you. Basically, you need to do your homework, but we will be right there to support you along the way! When we say **read it, learn it, live it** we really mean it on this site and assume that you will abide by that principle.

Additionally, I expect that you will be pleasantly surprised by the personal support and interactions from me, as well as from each of the caring individuals that are a part of Holistic Health International, LLC. I think you will be touched by the level of caring, love, and hope that you will learn to expect from all of us. However, you may be overwhelmed with the volume of information and products, and perhaps a bit daunted by it at first. Please do not hesitate to connect with our amazing customer support team with any questions or concerns you may have.

With Love, Hope & a Hug,
Dr. Amy

Contact for Discussion Group: Erin Griffin is our main Discussion Group Moderator
Email: griffkoom@verizon.net OR Erin.griffin@holistichealth.com
Discussion Group Signature: griffkoom

Phone Contact for the Office: (207) 824 8501 | (800) 768 8744 | Monday through Friday, 9:30AM to 5:30PM EST

Read Dr. Amy's *Feel Good Nutrigenomics: Your Roadmap to Health* Book

Online Copy: CLICK HERE
Hard Copy: CLICK HERE

Within this book, Dr. Amy gives an overview of how she approaches complex health issues by looking at the genetics of your nutritional pathway, infectious diseases, and environmental toxins. Then, Dr. Amy discusses how all of these elements overtime can interact and create health concerns. She goes on to describe how you, with the guidance from your health care professional, can address those issues. Within this book, you will also find a general overview of what SNPs* are and what The Yasko Protocol is all about before you really dive in. Dr. Amy considers this book as a prerequisite to reading *Feel Good About your SNPs* as it includes more basic concepts to help you understand the complexity of SNP interactions.

***What Exactly are SNPs?**

SNPs (Single Nucleotide Polymorphisms) pronounced "snips"

The first step that emerged from the Human Genome Project identified genes associated with a particular health condition. The next step would be to use this information and look for the presence of genes that can cause health issues in an individual person. Rather than looking at complete gene profiles, it is also possible to look at particular changes in the "spelling" of your DNA in only specific areas of interest. In this way, you can more quickly get a sense of known genetic weaknesses. Companies that offer this service enable you to look at genes of interest that may affect your susceptibility to heart disease, inflammation, detoxification or simply your ability to absorb nutrients. These tests are available using saliva samples, cheek swabs, as well as blood samples.

In order to find relationships between genetic changes and the susceptibility to health conditions, this testing is done utilizing single nucleotide polymorphisms, otherwise known as SNPs (pronounced "snips"). This process systematically compares genomes of those individuals with health conditions to the corresponding DNA of the population. To identify a SNP is a very arduous and time consuming process as there may be 400 or more genes in a shared region, making it difficult to identify changes and trends. However, once it has been identified, making practical use of this information is quick and straightforward.

*More details about SNPs: Dr. Amy's book *Feel Good About Your SNPs* + her FREE online presentation

This is a test that you will need to run only once in your lifetime. Your DNA will not change so, once you have Nutrigenomic Test results, those will not change over your entire lifetime. Unlike the follow up Biochemical Testing you may consider running to routinely check that your supplementation plan is making an appropriate change to better your health, a Nutrigenomic Test focusing on The Methylation Cycle* is something you will run only one time. You will work with your doctor to determine supplementation based on these SNPs for the rest of your life. For this reason, Dr. Amy feels that everyone should run a DNA SNP test if possible to have the data you need to optimize your supplement choices overtime with your own health care professional.

For any test questions, please reference the "Test Forum" section (to view this link, please signup/log into the Discussion Group) within the Discussion Group or contact our customer support.

With respect to SNP testing, there is one **critical point** that Dr. Amy feels is extremely important that everyone understands: There are approximately 25,000 genes in the human genome however, Dr. Amy personally believes in only looking at SNPs that are in well-defined pathways where it is clear how to add nutritional support to bypass imbalances. Having a laundry list of SNPs without a way to use nutritional support is not consistent with the way she approaches supporting your journey to better health. As such, please note that whether you have a test that gives you 1000 or 5000 SNPs, this is still only a fraction of the total number of genes in your body. For further information on this subject, **please view the note from Dr. Amy at the end of this section.**

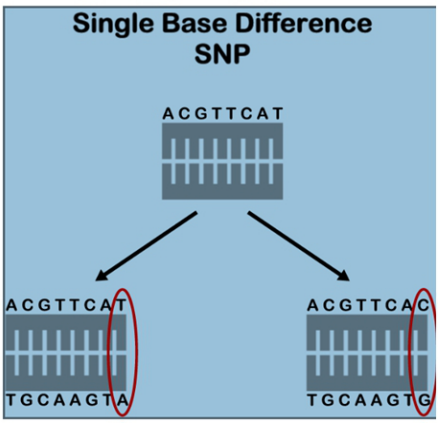
How to Read your Nutrigenomic Test results:

There are two copies of each gene that we are looking at in the profile, one copy comes from each parent.

- **Homozygous**: When both copies have a particular SNP or mutation (in other words when both copies are identical) with either + + or - -
- **Heterozygous**: When one copy that is + for the change and the other is - for the change

The + and - designations themselves refer to whether or not the gene has a change from what is considered "normal". If there is a change from what is considered "normal" then it is termed as a plus (+). No change is designated by a minus (-) sign. The definition of what is "normal" can vary from lab to lab and it will depend in part on what the lab uses as a reference database. This is why you are also given the **call letter** for each SNP. The call letter tells you what base was seen by the lab at a precise location on the gene.

For example, when looking at the MTHFR gene, the particular SNP we are interested in is the C677T. The lab is looking at position 677 in the DNA for a change from a C to a T. If there is a change, then the **call letter** will show a T and **the designation** will be a plus (+). If there is no change, then the **call letter** will be C and the designation will be a minus (-). If a different lab considers the change to a T as "normal", then they might show a T in position 677 as a minus (-), as their reference database may feel that it is normal to have a T in that position. This is why the **call letter** is so important. In cases where there is a discrepancy from one lab to another, the actual **call letter** will let you know what base was seen at a precise location. This enables you to be certain that tests run from different labs gave the same actual experimental result even if their reference standard for a "normal" change was different.



Assume the following scenario as an example: Dr. Amy is 5 feet 3 inches tall, her height will be equivalent to the call letter in this analogy as it is a precise measurement. If she compares her height to that of her children, Dr. Amy is taller than her youngest, the same height as her eldest, and shorter than her middle child. Using Dr. Amy's daughters as a reference base, Dr. Amy would consider her own height as average. However, if she compares her height to that of the rest of the population of her hometown, Dr. Amy is actually quite short since many of the individuals in her town are very tall. Using the + + and - - designations, she might be + - if the reference database was to her children, or + + if the reference database was to her hometown. In either event, Dr. Amy's height by precise measurement is 5 feet 3 inches and that will not change. Knowing the lab value allows Dr. Amy to compare her height to other databases in the future.

Guide to Minus (-) and Plus (+) Results:

- Minus (-) represents no mutation, in other words considered "normal"
- Plus (+) represents a mutation, in other worse not the standard / not "normal"
- Minus Minus (- -) indicates there is no mutation: Homozygous
- Plus Minus (+ -) indicates there is one mutation: Heterozygous
- Plus Plus (+ +) indicates there is a double mutation: Homozygous

Guide to Color-Coded Results:

- A red background indicates a greater level of support is needed
- A yellow background indicates that support is needed, but to a lesser degree than red
- A green background indicates that there is little to no support needed

Please note: The results column is color coded to correspond with the level of the support needed, so you may see some + - in red. For questions that you maybe have about your results, please utilize the discussion group at www.Ch3Nutrigenomics.com and, as always, consult with your health care professional.

A Note from Dr. Amy about DNA Nutrigenomic Testing:

Focusing on 30 SNPs

While there are thousands of genes and SNPs that I could look at, for my health program I have chosen to focus on the 30 SNPs that are part of a nutritional pathway in the body. It is not a panel that looks at specific genes that are involved in cancer or various disease states. Rather, it is a panel that looks at a natural nutritional pathway that is central to overall health and wellbeing. While many DNA panels work on the 'more is better' philosophy, I do not. Even if you ran a panel that looks at more than the 30 key SNPs I review, it is still only a small fraction of the total genes and SNPs in your body as you have about 25,000 genes in your body, some of which may have SNPs or mutations that impact their function.

Sharing Personal Information

I do have some ethical concerns with the 'more is better' approach of looking at a multitude of SNPs in your DNA. It has been stated that some of these companies are focused primarily on future research projects by sharing your data with other laboratories. I am **not**

sharing or selling your data, the only purpose of the SNP test from the panel I designed is for me to place it in your personal file so I can refer to it when I look at Biochemical Test results that you run. The laboratory that runs my SNP panel does **not** store any patient information and the blood or cheek swab samples are de-identified and discarded after 60 days: "Communication that occurs between our laboratories points to the Lab ID number – not patient name", in addition, "Genetic tests are handled in a confidential manner, like all other personal health information. Test results are released to the ordering health care provider, and to those parties entitled to them by state and local laws, or to a person whom you have specifically authorized by signing a written release" (https://www.doctorsdata.com/online-privacy/).

Conversely, some of the 'more is better' SNP tests come from companies that are able to offer a discounted price as their ultimate aim is to gather genetic information. It appears that they absorb some of the cost of the test itself in order to have a larger number of individuals ordering the tests so that they can gather more information, which is not kept confidential. A board member of one of these companies has publicly stated: "The long game here is not to make money selling kits, although the kits are essential to get the base level data…Once you have the data, [the company] does actually become the Google of personalized health care[…] The company has lowered the price of the kit again and again, most recently from $299 to a mere $99, practically making it a stocking-stuffer. All the better to induce volunteers to give the data it so desperately wants" (Zhang, July 2018. The Atlantic). It may not matter to you that your data will be shared, just be sure you are making an informed choice.

Please note that if you cannot afford a more targeted and confidential SNP panel and have chosen a lower cost option, that is absolutely okay. I would rather have some SNP data, even if some of the key SNPs are missing, than no data at all. That is why I have set up my protocol to include data from any panel. My goal is to have the most information in your file so that I can do the best possible job of making suggestions for you and your personal doctor to consider implementing to achieve optimal health.

Problem without a Solution

My final concern about 'more is better' SNP panels is that they often tell you there is an imbalance, yet they have no knowledge of nutritional paths around the issue identified. They also do not look to assure you that just because a SNP has been found, that it is not necessarily a cause for panic*. I only believe in looking at DNA profiles and SNPs that yield information that can be addressed with nutrients. I do not believe in testing just for the sake of testing, which is why I am not a 'more is better' advocate in terms of the number of SNPs data on a given test. I believe that DNA testing without any knowledge of how to address the issues that are uncovered is unethical. I believe in targeted testing in a defined nutritional pathway so you have options for natural supports to bypass imbalances that are found and make a positive difference.

The beauty of looking at targeted SNPs in The Methylation Cycle is that it is a nutritional pathway, so you can consider natural products to help support imbalances or SNPs that are found in this pathway. Nutrigenomic Test results that look at SNPs in your DNA should help to put your mind at ease by giving you suggestions that you can act on. Nutrigenomics is a form of Genetic Testing that supplies information that can translate into positive constructive action. I see the ultimate goal of Nutrigenomic Testing to serve as a guide toward proper supplementation to bypass genetic weaknesses identified by SNP results. I believe in running follow up Biochemical Tests to be sure that the nutritional supplements added have the desired positive impact. My ultimate goal is to use Nutrigenomic Testing as a guide to proper supplementation to bypass genetic weaknesses, under the purview of your own doctor.

*More details about SNPs: Dr. Amy's book *Feel Good About Your SNPs* + her FREE online presentation

*For a basic understanding of The Methylation Cycle, please view Dr. Amy's book *Feel Good Nutrigenomics: Your Roadmap to Health*
Online Copy: CLICK HERE
Hard Copy: CLICK HERE

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Start Step One Support

Start "Step One Support" within Your Roadmap to Health

Step One Support: GF/CF Diet, Limit Excitotoxins, Balance Gaba/Glutamate, Review the Methylation Support Sheet* for Basic Methylation Support, Add in Supports for Organ Systems as described in the Companion Guide on pages 15 to 26.

*Methylation Support Sheet: This support sheet includes links that lead you directly to the products ecommerce site and is available within Your Roadmap to Health.
*Your Health Companion: Dr. Amy's Health Companion is a FREE user friendly, personalized client portal to help support your journey to better health and wellness. Within this secure system, you can access your Client History Form, Supplement List, Test Results, and more! This wonderful system will help to organize your important information for years to come, saving all files within our client portal for you to access and reference easily.
To Learn More: CLICK HERE

While you may already be on the GF/CF diet (which Dr. Amy recommends), there is an additional step to the diet that needs to be made in order for the inflammatory process to abate and the recovery process to begin. This additional dietary step/intervention is to remove/reduce excitotoxins from the diet and from supplements as well.

Excitotoxins are: Glutamate, Glutamic Acid, MSG, Glutamine (which converts to Glutamate), Aspartate, Aspartame, NutraSweet, and Cysteine. Foods that are especially high in Glutamate are: Soy, Peas, Mushrooms, Tomatoes, Beets.

A diet high in fermented foods and/or high protein may also contribute to this issue. It is important to be conscious of the total load of Glutamate and to think of your ability to tolerate more Glutamate as if your cup is already full to the brim and about ready to overflow.

Dr. Amy feels that it is important to balance Glutamate and Gaba in part by pulling down Glutamate levels that are too high. Products you can consider for help with this process include: BeCalm Spray, Ku Shen Tea, Gaba Balance, Nerve Calm Nucleotide Blend, Resveratrol Spray, Pycnogenol, and Grape Seed Extract.

Please note that it is not necessary to use all of these. Which products you choose will depend on your health care professional's opinion considering how much of an issue Glutamate is for your body and which supplements your body will respond well to.

Also, Glutamate works with Calcium to cause excitotoxicity, so keeping Calcium in balance with products such as Zinc, low doses of Lithium, and low doses of Magnesium can be helpful.

What is not included in The Yasko Protocol: Glutamate/Glutamine. The following are not included in The Yasko Protocol in high doses: Calcium, TMG/Betaine, Folate, Folinic, 5 Methylfolate, or B6. Those who follow the DAN protocol, a diet high in fermented foods, a diet high in protein, or those who have been using high doses of 5MTHF, chelating agents and/or higher doses of Methyl B12, may find that they especially need to balance Lithium, get Gaba/Glutamate supports and extra organ supports on board.

Dr. Amy's All In One supplement is a custom general vitamin, taking into account the imbalances she has seen on thousands of tests for over a decade. Dr. Amy believes All in One can help lay the nutritional groundwork for essentially everyone on the program, including those who are sensitive to Sulfur and/or Methyl Donors, along with those who are MTHFR+, CBS+, etc. All in One contains **very low** dose Lithium, the preferred forms of several important key minerals, and **very low** dose supports for The Methylation Cycle. This helps to ensure that The Methylation Cycle can function to some degree at a very low level regardless of your SNP profile.

Suggested use is to start with a single capsule and gradually work up to the suggested 3-4 capsules per day, as tolerated. Although opening the capsule may expose the ingredients to oxygen, it should be fine for those who are younger, sensitive or new to the program who need to start with just a sprinkle.

For more information on All in One ingredients and rationale, please reference the Discussion Group (to view this link, please signup/log into the Discussion Group) or contact our customer support.

We all need organ supports including Adrenal, Kidney, Pancreatic, and Liver. Those with certain genetics, certain Biochemical Test results and/or a history of Chelation may need extra supports. Organ supports to consider include MTHFR A1298C+ Liver Support, VDR / FOK Pancreatic Support, Ultimate B Complex, Special Digestive Enzymes, Intact Multigland, and Kidney Beef.

Next, you can work with your health care professional to get some Basic Methylation support in place. Start with the Basic Methylation Support Sheet*, looking at the use of Phosphatidyl Serine Complex, along with SAMe (if it is tolerated), VitaOrgan, and DHA Neuromins.

*Basic Methylation Support Sheet: This support sheet includes links that lead you directly to the products ecommerce site and is available within Your Roadmap to Health.

Low doses of Lithium supports are also important for everyone to consider. Both All in One and the BeCalm Spray are excellent sources for this purpose. The doses are well tolerated even for those just starting The Yasko Protocol. This low level of Lithium may not be sufficient to support those who have very low Lithium levels on a Hair Elements Test (HE). Once you have received your test results to check that your Lithium levels are in balance by running a Urine Toxic & Essential Elements Test (UTEE) and Hair Elements Test (HE), work with your doctor on additional low dose Lithium supports as needed. Options to discuss with your health care professional for additional Lithium support include Lithium Orotate capsules and Lithium Drops. If needed in unique cases, prescription Lithium can be obtained from your doctor. Where Lithium plays a role in B12 transport, if you start to add too much B12 before Lithium is in balance, you run the risk of further depleting Lithium levels.

For any of these supports mentioned, the "low and slow" method is suggested. Dr Amy considers a "sprinkle" a bonafide dose. Just by stopping a supplement or changing your diet you may see detox, consider running ongoing Biochemical Testing to recognize these changes and implement appropriate supplementation to control it. As always, work and consult with your own health care professional. Remember, this is a marathon not a sprint!

A Note from Dr. Amy about Supplementation:

Choices I make in terms of supplements are based on their impact on test results and this is a unique approach that is not taken by others who are solely looking to sell supplements. I see supplements as a much needed tool for health, not as a commodity. I see the whole person, not just a test file. I see your health history and future health goals. I truly feel passionate about supporting your health goals for both yourself and your loved ones. When I talk about supplements please understand I am not making claims, nor stating that any supplement or herb will cure a given health condition. My concern about supplement source is related to the fact that I find it a true privilege to be a part of so many lives and to be given the opportunity to help others. I receive emails and test results from individuals daily who are following The Yasko Protocol where their lives are being changed in a really amazing way. Those who follow my protocol as designed and use the correct products really do see wonderful results. When I see such progress, it is due in part to supplements being added as indicated by the suggestions I include based on test results, and when tests were done on a regular basis. This is what I want to see for each and every one of you, this is why I do what I do each day. I hope that you understand my focus on supplement source and quality comes from a place of caring. I always want to see positive progress on your follow up tests, I want to hear stories of success from each and every one of you, and I want all of you to be able to achieve the health you are looking for. Please see my *Feel Good Supplements Guidebook* (everyone should receive one free copy automatically when they order from **www.HolisticHeal.com**) to learn more about the importance of this topic.

Hair Elements Test and Urine Essential Element Test

Order a Hair Elements Test (HE) and if financially feasible, also order a Urine Essential Element Test (UEE) to ensure your Lithium levels are in balance. Please recall that Lithium is important for B12 transport.

For any test questions, please reference the "Test Forum" section (to view this link, please signup/log into the Discussion Group) within the Discussion Group or contact our customer support.

Lithium

Lithium not only plays a role in mood, Glutamate control and limiting aggression, but also has been shown to be involved in B12 transport. Many adults (as well as individuals who are MTR A2756G+) tend to have lower levels of Lithium as judged by Hair Elements Test (HE). Supporting with higher levels of B12 before having ascertained that Lithium is in balance may lead to further depletion of Lithium levels. For this reason, Dr. Amy highly suggests running a Hair Elements Test (HE) and/or a Blood Lithium Test (that can be run through your health care professional), along with a Urine Essential Element Test (UEE) to assess the Lithium levels in your system. If

Lithium levels are low in hair, blood or urine, please consider additional Lithium supplementation with your doctor before moving onto B12 support. Similarly, if very high levels of Lithium excretion are showing up on your UEE Test, one should consider additional Lithium supports with their health care professional prior to transitioning to B12 support. Sources of Lithium support can include BeCalm Spray, low doses of Lithium Orotate, and All in One. The level of support needed should be determined by a combination of running Biochemical Tests as well as a consultation with your personal health care professional.

Work on increasing B12 while continuing to track levels of Lithium to be sure it stays in balance while increasing B12. Running a HE Test consistently can help monitor Lithium levels while increasing B12 supports.

Determine Your Ideal Form of B12

Once your Lithium levels are in balance and Basic Methylation is in place, increasing B12 support will be the next step. In conjunction with paying attention to your B12 levels, you can begin to customize your supplement plan based on your test results. Your Nutrigenomic Test results can guide you through individualizing your supplementation choices. While we all need B12, each person is unique in which form of B12 will best suit their body. If you have chosen to add All in One or/and Ultimate B Complex to your supplements, you are already getting some low doses of B12 support. The forms of B12 in both of those vitamins are designed to be tolerated by all, but now it is time to add in some specific B12 supports based on your Nutrigenomic Test results. The chart below will help you to determine which form of B12 might be best tolerated by your system.

Please note that while this chart can help guide you to choose the type of B12 support based on Nutrigenomic Test results, it is also important to pay attention to what your body is telling you. It is important to know that individuals who tend to have a more difficult time with any supplements that can trigger detox may also have issues with Methyl B12. As such, if you are having trouble tolerating Methyl B12, then listen to your body's reaction and instead discuss with your doctor about switching to Hydroxy B12 with some Adenosyl B12 as an alternative approach to B12. For a more detailed description of the different types of B12, along with references for their uses, please view the content after the chart below.

COMT V158M	VDR Taq	B12 Types that Should be Tolerated
- -	+ + (TT)	All 3 types of B12
- -	+ - (Tt)	All 3 types with less Methyl B12
- -	- - (tt)	Hydroxy B12 and Adenosyl B12
+ -	+ +	All 3 types with less Methyl B12
+ -	+ -	Hydroxy B12 and Adenosyl B12
+ -	- -	Hydroxy B12 and Adenosyl B12
+ +	+ +	Hydroxy B12 and Adenosyl B12
+ +	+ -	Hydroxy B12 and Adenosyl B12
+ +	- -	Mostly Hydroxy B12

Why it is so important to have a form of B12 that you can tolerate:

- Vitamin B12 is a water soluble vitamin, this means that it does not stay in the body for a long period of time and that more frequent support with B12 may be needed to maintain healthy B12 levels in the body.
- Vitamin B12 is important for energy, balance related sports, endurance sports, healthy red blood cells, memory, among other roles in the body.
- Vitamin B12 can be depleted by drinking alcoholic beverages, a poor diet, certain medications, and simply just as we age.
- Lack of B12 has been associated with fatigue, alcoholic liver disease, anemia, cancer, ulcers, dementia, neural tube defects, depression, and memory loss.
- Higher levels of B12 correlate with improved balance, energy, and endurance in athletics.

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Different types of B12 work best for different people:

Vitamin B12 (also called Cobalamin) can include Hydroxy B12, Methyl B12, Cyano B12, and Adenosyl B12. Many vitamins (including B12) are not active in the form in which they are normally found in food. Instead, the body needs to convert the B12 into a form that it can use directly. B12 is needed for the proper functioning of a number of different enzymes in the body however, not all types of B12 are equal and not all types of B12 can be easily changed to what is needed for critical reactions in the body. Hydroxy, Methyl, and Adenosyl are all forms of B12 that are used directly by reactions in the body. Cyano must be converted for use in the body and as the name suggests, Cyanocobalamin contains a Cyanide Molecule.

Methyl B12:

Methyl B12 can be used in the body, though it cannot be tolerated by everyone. Those who get jittery from caffeine may not react as well to Methyl B12. Many adults do not do as well with Methyl B12 in spite of their nutrigenomics and so, it is suggested to choose an alternate form.

Adenosyl B12:

Adenosyl B12 is a special form of B12 that is important in the energy cycle in the cells of your body. It is important to have Adenosyl B12 however, please know this form of B12 is not as versatile as other forms of B12. As such, it can be used in lower doses.

Hydroxy B12:

Hydroxy B12 (or Hydroxycobalamin) is a unique form of vitamin B12 which is more easily converted to the form that is used for reactions in the body. This might cause you wonder why all products would not simply use high dose Hydroxy B12 in their formulations. Hydroxy B12 is more difficult to work with, harder to keep in an active form, and more expensive than some other forms of B12 (such as Cyano B12). For these reasons, many other products do not contain Hydroxy B12 and instead use Cyano B12.

Cyano B12:

Cyano B12 contains a Cyanide Molecule. As such, when you take Cyano B12, your body must first turn it into Hydroxy B12 in order to use it. Your body then must find a way to get rid of the toxic Cyanide Molecule. It is important to note that Cyanide is a poison, even if the rest of the B12 molecule is good for you and the body actually uses up Hydroxy B12 in order to detoxify Cyanide. So, not only is Cyano B12 not the form your body ultimately needs, but taking higher doses of Cyano B12 may actually deplete your body's natural levels of Hydroxy B12. This may cause you to wonder why anyone would use Cyano B12 if it can be toxic. In low doses, Cyano B12 may be helpful for the eyes, but for the most part Cyano B12 is used because it is much less expensive and a form of B12 that is easier to keep stable when stored.

For a complete list of B12 Supports: CLICK HERE

Dr. Amy Yasko
Ph.D, NHD, AMD, FAAIM, HHP, CTN

Start Full Methylation Support

Start "Full Methylation Support" within Your Roadmap to Health

Full Methylation Support: Methyl Folate 5-MTHF Drops, Folinic+ Capsules, Additional B12 Supports (type of B12 depends on SNPs), and also Review the Methylation Support Sheet*

Please Note: When starting the next step of Full Methylation Support, this does **not** mean that you should stop any of the steps within Step One Support (view the above section titled "Start Step One Support within Your Roadmap to Health" for more details). Specifically, use **both** Basic Methylation Supports **and** Full Methylation Supports

*Methylation Support Sheet: This support sheet includes links that lead you directly to the products ecommerce site and is available within Your Roadmap to Health.

*Your Health Companion: Dr. Amy's Health Companion is a FREE user friendly, personalized client portal to help support your journey to better health and wellness. Within this secure system, you can access your Client History Form, Supplement List, Test Results, and more! This wonderful system will help to organize your important information for years to come, saving all files within our client portal for you to access and reference easily.
To Learn More: CLICK HERE

Dr. Amy Yasko
Ph.D, NHD, AMD, FAAIM, HHP, CTN

Biochemical Testing

Biochemical Testing measures the amount or activity of a particular enzyme or protein from a sample of urine, stool, or hair. The Biochemical Tests help to assess progress with methylation as well as nutrient absorption and neurotransmitter levels. As depicted on Your Roadmap to Health, Biochemical Testing is an ongoing tool that you can use to assess your current progress and to know when and how to proceed. Please refer to the Companion Guide on pages 27 to 53.

Dr. Amy uses Biochemical Testing in conjunction with DNA SNP Data to customize her supplement suggestions specifically for your unique needs. Follow up Biochemical Testing can be done routinely to check that your supplementation plan is making an appropriate change to better your health. Unlike Genetic Tests, Biochemical Test results will change over time. The goal is to use the knowledge of your genetics to make informed decisions on how to supplement and bypass weaknesses in your system and then to use regular Biochemical Testing to monitor the progress of your supplementation to bypass mutations.

When Dr. Amy completes her client file review on a test you've run, she includes a sheet that offers suggestions for the next Biochemical Test to run based on what your current test results are. These test suggestions from Dr. Amy are there to help guide you and your health care professional through The Yasko Protocol. Dr. Amy also makes suggestions within her book *Feel Good About Your SNPs* about specific Biochemical Tests. Within her book, Dr. Amy discusses which Biochemical Tests will be of most value to you depending on your specific SNPs.

Also, for further information on Biochemical Testing, please view Dr. Amy's free online book: *Feel Good Biochemistry*. This resource goes through each biochemical test and explains how Dr Amy views the results of those tests and details suggestions she would make on a test. This is an amazing resource for you and your doctor to be able to run tests and get her viewpoint on the results.

It is suggested to run a UTM and UEE, a UAA, and a HE when starting the program, during Step One Support and/or adding Basic Methylation Supports. Please refer to the Companion Guide on pages 55 to 58 for a basic understanding and explanation of these test results, along with viewing *Feel Good Biochemistry*.

- HE can be run while waiting for genetics results and will help to assess detox, Lithium and other essential element levels.
- UTM and UEE can be run while waiting for genetic results and will help to assess minerals levels, determine detox and creatinine.
- UAA can be run while waiting for genetics results and will help to assess Ammonia, Taurine, Glutamate, Gaba and other amino acid levels.

Please note that Dr. Amy likes the OAT Test and the NC Test to be run together for those who have concerns about stress, behavioral patterns, mood, and issues with attention.

Also, Dr. Amy occasionally will graph your hair, urine, and fecal toxic tests as an additional way to monitor your progress.

For any test questions, please reference the "Test Forum" section (to view this link, please signup/log into the Discussion Group) within the Discussion Group or contact our customer support.

Dr. Amy Yasko
Ph.D, NHD, AMD, FAAIM, HHP, CTN

Understanding Your Genetic Results: Priority of Mutations

Once you have reviewed your Nutrigenomic Test results and have Step One/Basic Methylation Supports in place, please refer to:

Feel Good About Your SNPs book + the Corresponding FREE Online Presentation

The Companion Guide on pages 60 to 63

The Genetics 101 post to understand your results (to view this link, please signup/log into the Discussion Group)

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Your SNP Results

The following section is comprised of specific details about the SNPs identified on your DNA test results. You will be able to review your specific SNPs within a chart format (generated by www.KnowYourGenetics.com) which will include supplement suggestions for your consideration provided by Dr. Amy's experience and expertise. Above each chart, you will also find a description of the characteristics of each SNP, written personally by Dr. Amy.

The supplement lists you will see within this packet include important starting products based on your SNPs you may want to consider adding to support the function of the genes containing those SNPs. You do **not** need to use every supplement listed; these are simply options to discuss with your own health care professional. Dr. Amy feels these are essential products to review with your health care professional with the goal of integrating them into your supplement plan. Upon running follow up Biochemical Tests to assess your progress, Dr. Amy can then supply further supplementation options for your consideration within your client file review.

Each section also includes a list of Biochemical Tests that can be used to monitor the impact of the supplements you have added. Dr. Amy is a strong believer in using data to assess how well a supplement program is working for you. Running follow up Biochemical Tests helps to ensure that the supplements you are adding to address SNP imbalances are having the effect you and your health care professional desire. It is important to note that while your DNA and SNPs will not change over time, your Biochemical Test results will change. As such, these tests can reflect your progress in overcoming imbalances through the use of supplementation.

While reviewing your results, you have the opportunity to create a Personalized Shopping List by selecting which products you would potentially like to purchase. After the last page of your results, there is a "submit" button that will create a PDF with the selected items of interest and their corresponding hyperlinks for you to reference and consult with your health care professional. As always, consult with your health care professional.

If you begin to feel overwhelmed by your results, please read Dr. Amy's *Feel Good Nutrigenomics: Your Roadmap to Health* book (available online or in a hard copy) for the basics. Also, please note that Dr. Amy's *Feel Good About Your SNPs* book and her Corresponding FREE Online Presentation can be helpful for further details:

"I strongly believe that knowledge is power, I find that people are often afraid of their SNPs and I would like to support the shift from fear to understanding. My goal in offering this presentation is to help put your minds at ease, giving you more tools to support your personal journey. I hope that by the end of my presentation, in addition to reading my book, you will begin to have a better understanding of the interactive picture between your SNPs and Methylation Cycle, allaying any internal concerns," Dr. Amy

Disclaimer:

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Dr. Amy Yasko
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Guide to Color-Coded Results:

- A red background indicates a greater level of support is needed
- A yellow background indicates that support is needed, but to a lesser degree than red
- A green background indicates that there is little to no support needed

John_Doe_MPA_06.16.21
DOB: 08/15/1980

SNP	Gene	Variation	Result	Call
RS4680	COMT	V158M	-/-	GG or G
RS4633	COMT	H62H	-/-	CC or C
RS769224	COMT	61	-/-	GG or G
RS731236	VDR	Taq	Tt	Hetero
RS2228570	VDR	Fok	FF	CC or C
RS6323	MAO A	R297R	-/-	GG or G
RS3741049	ACAT	1-02	+/-	Hetero
RS1801133	MTHFR	C677T	-/-	CC or C
RS2066470	MTHFR	3	+/-	Hetero
RS1801131	MTHFR	A1298C	+/+	CC or C
RS1805087	MTR	A2756G	-/-	AA or A
RS1801394	MTRR	A66G	+/+	GG or G
RS10380	MTRR	H595Y	-/-	CC or C
RS162036	MTRR	K350A	-/-	AA or A
RS2287780	MTRR	R415T	-/-	CC or C
RS2303080	MTRR	S257T	-/-	TT or T
RS1802059	MTRR	11	+/-	Hetero
RS585800	BHMT	1	-/-	AA or A
RS567754	BHMT	2	+/-	Hetero
RS617219	BHMT	4	+/-	Hetero
RS651852	BHMT	8	+/+	TT or T
RS819147	AHCY	1	-/-	AA or A
RS819134	AHCY	2	-/-	TT or T
RS819171	AHCY	19	-/-	AA or A
RS234706	CBS	C699T	+/-	AG
RS1801181	CBS	A360A	+/-	Hetero
RS2298758	CBS	N212N	-/-	CC or C
RS773115	SUOX	S370S	-/-	No Support Needed
RS1979277	SHMT	C1420T	+/+	AA or A
RS1799983	NOS	D298E	-/-	GG or G

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ACAT + - or ACAT + +

ACAT is the abbreviation for the enzyme *acetyl coenzyme A acetyltransferase*. It is in the part of the pathway that feeds into the Krebs energy cycle so it is a factor in generating mitochondrial energy.

Biochemical test results that may indicate imbalances in ACAT include particularly high methionine on a UAA test, high cholesterol, low lithium, high levels of ketones, high pyruvate, high lactic acid. The observed higher levels of methionine may also contribute to the high cholesterol noted for ACAT + and exacerbate that situation (Hirche, May 2006, Br. J. Nutr). ACAT plays a role in cholesterol and other lipid balance in the body, helping to prevent the accumulation of excess cholesterol in certain parts of the cells in the body. ACAT is also involved in energy generation in the body. It is involved in helping to allow protein, fats and carbohydrates from food to be converted into an energy form that can be used by your body.

The job of this enzyme is to take two of the compound acetyl CoA and convert it to acetoacetyl CoA. If ACAT is overactive, then more acetyl CoA is used up than would be ideal, leading to lower levels of acetyl CoA and excess levels of acetoacetyl CoA.

Acetyl CoA is needed to make acetylcholine. This is an important compound in the body that is involved in learning and memory. Individuals with Alzheimer's are reported to be low in acetylcholine. Acetylcholine is a key neurotransmitter in the nervous system and plays a role in activating muscles. Certain nerve toxins, such as Sarin, do their damage by tampering with acetylcholine. Depletion of acetyl CoA, resulting in lower acetylcholine might be expected to impact muscle tone, learning and memory.

Overactive ACAT levels not only can potentially decrease the level of acetylcholine but would also increase the level of acetoacetyl CoA. This compound goes on to create high levels of ketones in the body as well as increasing the pathway to cholesterol. The buildup of ketones is not ideal and even mild levels of ketones can cause a 'foggy' mental feeling, headaches, weakness and fatigue. Certain microbial infections, such as *H.pylori* can also increase ketone levels, and increases in ketones are observed for those using a ketogenic diet. Combining an ACAT SNP, with the presence of *H.pylori* and a ketogenic diet may lead to levels of ketones that are really not ideal.

Increases in ACAT also result in high levels of cholesterol (Ta Yuan Chang, July 2009, Am J Physiol Endocrinol Metab.). This not only has health implications, but high cholesterol has been associated with low lithium. Older studies show that high cholesterol could be correlated with changes in lithium excretion (Hunt, March 1960, Cardiovasc Drugs Ther.). This would fit with my personal observations that those with ACAT + status often have high level lithium excretion and high cholesterol levels. It is possible this is a compensatory mechanism by the body as lithium aids in B12 transport, and I have observed repeatedly that low lithium results in low cobalt (as a measure of B12) in both hair and urine. A deficiency of B12 has impacts on the energy cycle which may allow for conservation of acetyl CoA via an impact on enzymatic reactions (Frenkel, Nov. 1974, J. Biol. Chem.). Increased ACAT activity would not only lead to increased cholesterol but can deplete the internal pool of acetyl CoA.

In addition to decreased lithium, there are also reports of lower levels of potassium in cells as a consequence of higher cholesterol levels (Hunt, Jan. 1986, Hypertension). This would fit with what I have seen in terms of low lithium and low potassium on Hair Elements (HE) tests for individuals who are ACAT +. Low potassium may be a factor in aggression and outburst of rage secondary to its impact on rubidium levels.

The high cholesterol levels noted for those who are ACAT + and for many who have low lithium may be a particular issue in terms of certain microorganisms. High cholesterol can create an environment that is conducive to the growth of a number of species of *Mycoplasma*. In fact, most species of *Mycoplasma* have been shown to actually require cholesterol for growth. "The results provide experimental support for the view that the large majority of the established *Mycoplasma* species require cholesterol for growth" (Razin, May 1970, J. Bacteriol.).

Mycoplasma has classically been thought of in terms of lung infections and can create imbalances in the TH1/TH2 immune response (Segovia, May 2017, J Immunol). However, the impact of *Mycoplasma* goes far beyond lung infections. Antibodies produced in response to *Mycoplasma* can cross react with components in the body that may allow for demyelination and mimic certain demyelinating conditions. (Ang, Sept 2002, J Neuroimmunol. ; Tan, Sept 2003, Pediatr Neurol.). In addition, *Mycoplasma* has been associated with over production of mast cells and may play a role in Mast Cell disorders as well as being tied to Fibromyalgia and Chronic Fatigue syndromes (Nicolson, 1998, Biomedical Therapy).

Mycoplasma is also implicated in pediatric neuropsychiatric conditions, playing a role in PANDAS/PANS (Pediatric Autoimmune

Neuropsychiatric Disorders Weintraub, April 2017, Discover). While we traditionally think of *Streptococcus* as the offending organism for PANDAS, it is important to also look for and rule out *Mycoplasma* when PANDAS/PANS is suspected. This is particularly true for those who are ACAT + and/or show high cholesterol and low lithium on biochemical tests. Certain membrane components of *Mycoplasma* are shared with *Streptococcus* (Plackett,Sept 1967, Biochem. J.) and *Mycoplasma* has been listed as a possible organism associated with non-*Streptococcal* PANS (Cooperstock, 2017, J Child Adolesc Psychopharmacol).

Aside from PANS, *Mycoplasma* can play a role in a range of neurological and visual conditions and may even be implicated in psychosis (Guleria, Aug 2005, J Lab Clin Med.; Tsiodras, Dec 2005, J Infect.; Narita, Sept 2009, Pediatr Neurol.; Nunes, June 2011, J Neurol Sci.; Shiihara, May 2010, Eur J Pediatr.; Thomas, Nov 1993, Arch Dis Child.).

Chronic bacterial issues, whether due to *Mycoplasma* or other organisms, can have secondary impacts on the thyroid, leading to imbalances in thyroid values (Kwakkel, May 2011, Neth J Med.; Burgi, Aug 1986, Endocrinology). Thyroid imbalances can impact weight, mood, sleep and behavior. Studies in animal models have found an association between mutations in ACAT and lower levels of T3 thyroid hormone. ACAT also plays a role in fat digestion and I often see imbalances in fatty acids on stool tests for those who are ACAT + along with higher levels of nonideal microbes on these tests. Some of the individuals on my program who seem to have trouble with weight management are in fact found to be ACAT + once we have completed SNP testing.

Key Supplements to Consider for ACAT + - or + +

- Ultra Dairy Digest
- Mitoforce
- L-carnitine
- Biotin
- Ultimate B Complex
- ACAT/BHMT caps for conversion of energy and addressing ketones
- Low dose lithium and potassium based on Hair Elements (HE) test results
- Special Digestive Enzyme
- Bactisolve (if tolerated and if no shellfish allergy) due to gut bugs
- CoQ10
- ACAT + nucleotide blend
- Basic Methylation Support

Biochemical Tests to Assess Progress for ACAT + - or + +

- Organix Comprehensive Profile test (OAT) to check lactate and pyruvate for conversion of food into energy cycle and check for ketones
- Hair Elements (HE) test to check for lithium
- GI360 test for gut bugs
- Urine Amino Acids test (UAA) for high methionine
- Cardiometabolic test or alternative for cholesterol levels
- Mycoplasma saliva and urine tests for the presence of Mycoplasma
- Thyroid test and Urine Iodine if thyroid or weight is a concern

SNP Results	Supports to Consider	Personalized Shopping List
ACAT + - or + +	ACAT/BHMT capsules	☐
	Ultra Dairy Digest capsules	☐
	Mitoforce capsules	☐
	L-Carnitine tablets	☐
	Biotin capsules	☐

	Ultimate B Complex capsules	☐
	Lithium Orotate capsules	☐
	Lithium Drops	☐
	Potassium drops	☐
	Potassium capsules	☐
	Special Digestive Enzyme capsules	☐
	Bactisolve capsules	☐
	Coenzyme Q10 spray	☐
	Coenzyme softgels	☐
	ACAT + nucleotide blend	☐
	Basic Methylation Support	☐

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BHMT 1,2,4,8 + - or + +

BHMT is the abbreviation for the enzyme *betaine homocysteine methyltransferase*. The pathway for BHMT is central to the "Short Cut" or "Basic" methylation cycle that I use as a starting point to help balance The Methylation Cycle. BHMT acts on the path to convert homocysteine to methionine via a route that does not require B12. This secondary route exists to convert homocysteine to methionine, utilizing the BHMT enzyme.

The BHMT pathway is one route around The Methylation Cycle to convert homocysteine to methionine. The longer route around the cycle (Full methylation) involves the MTR and MTRR genes. Decreased function of the MTR or MTRR or a lack of B12 will diminish the level of conversion of homocysteine to methionine via the long route/Full methylation enzymatic route; this puts more pressure on the BHMT pathway. Rather than using 5 methyl tetrahydrofolate and methyl B12 for this conversion, the BHMT enzyme utilizes TMG (betaine) or phosphatidyl serine as starting material for this alternative reaction. I choose not to use TMG as it can convert to DMG and shift to Full Methylation before I am ready to do so. I prefer to use PS/PE/PC complex and DHA to support BHMT SNPs. It is actually wise to consider adding extra PS to help to drive this reaction for those who are BHMT +.

While DMG works well to support language, it may be best to wait to add any DMG until this pathway is supplemented properly, as the DMG may be inhibiting this BHMT reaction to methionine. Certain combinations of SNPs may create a greater need for support for the BHMT part of the pathway relative to the MTR/MTRR route around the cycle.

There are several SNPs that can impact BHMT function. BHMT 1, 2, and 4 appear to have a less pronounced effect on BHMT activity than BHMT 8. Those who are BHMT 1, 2, or 4 + should still consider extra Basic or Short Cut Methylation Support, however those who are BHMT 8 + or + + may need to use extra support to compensate for the BHMT 8 SNP.

The BHMT conversion of homocysteine to methionine can be affected by stress, by cortisol levels and may play a role in ADD/ADHD by affecting norepinephrine levels. Those who are BHMT + seem to benefit from additional Short Cut/Basic Methylation Support.

SAMe can inhibit BHMT to slow down the short cut and help to make the shift to the long route around the pathway. While this may also help with ADD, it may be an issue for those who are BHMT 8 + along with MTRR + +. We are looking to achieve a balance between Basic/ short cut methylation and Full/long route methylation so that both are functioning simultaneously. SAMe aids in that balance by slowing down the BHMT route and regulates MTHFR in the reverse direction as well as increasing CBS activity. Those who are CBS + along with BHMT 8 + and MTRR + + need to be cognizant of the impact of SAMe on further increasing CBS activity.

Running UAA and OAT tests to look at methylation cycle intermediates is useful in making sure there is a balance of Basic and Full methylation pathways. High FIGLU would indicate not enough Full Methylation Support, high sarcosine and glycine may indicate too much Short cut activity. High methionine would indicate insufficient methylation cycle support in general and low methionine with high taurine indicates high CBS activity. In addition, in some cases BHMT 8 + + status can be associated with blood sugar imbalances. Those who are BHMT 8 may want to pay particular attention to chromium and vanadium levels as well as to check blood sugar levels once in a while.

Key Supplements to Consider for BHMT 1,2,4,8 + - or + +

- All in One
- Extra Phosphatidyl Serine Complex
  DHA
- Low dose lithium and potassium based on Hair Elements (HE) test results
- Attention nucleotide blend as needed
- Intact Multigland
- Stress nucleotide blend
- Ora-Adrenal
- BHMT 1,2,4 + nucleotide blend
- BHMT 8 + nucleotide blend
- Basic Methylation Support

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Biochemical Tests to Assess Progress for BHMT 1,2,4,8 + - or + +

- Comprehensive Neurotransmitter test (NC) to check epinephrine and norepinephrine levels for attention issues
- Hair Elements (HE) test to check for lithium so that extra B12 can be added
- HE test to check for excessive thorium as an indication of CBS imbalances
- HE test to check for dumping of vanadium and molybdenum as an indication of high taurine and sulfur that needs processing
- HE test to check chromium and vanadium levels for BHMT 8 +
- Urine Amino Acids test (UAA) to check relative level of methionine to taurine as a measure of The Methylation Cycle as well as sarcosine and glycine
- Organix Comprehensive Profile test (OAT) for FIGLU as a measure of The Methylation Cycle
- Cardiometabolic test for blood sugar markers or equivalent

SNP Results	Supports to Consider	Personalized Shopping List
BHMT 1,2,4,8 + - or + +	All in One capsules	☐
	Phosphatidyl Serine Complex softgels	☐
	DHA softgels	☐
	Lithium Orotate capsules	☐
	Lithium Drops	☐
	Potassium drops	☐
	Potassium capsules	☐
	Intact Multigland capsules	☐
	Ora-Adrenal capsules	☐
	Attention Support nucleotide blend	☐
	Stress Foundation nucleotide blend	☐
	BHMT 1, 2, 4 + nucleotide blend	☐
	BHMT 8 + nucleotide blend	☐
	Basic Methylation Support	☐

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CBS A360A + - or + + | C699T + - or + + | N212N + - or + +

The CBS enzyme (*cystathionine-beta-synthase*) acts as a gate between homocysteine and the downstream portion of the pathway that generates ammonia in the body. The types of CBS mutations that are identified on the SNP panel I designed are focused on CBS imbalances that cause this "CBS gate" to be left open; this "open gate" is not a neutral situation. The "open gate" can allow support that is added for the rest of the methylation pathway to be depleted, including any B12 that is used to address MTR and MTRR mutations. While there are some positive end products that are generated via the downstream portion of the pathway such as glutathione and taurine, there are also negative byproducts such as excess ammonia and sulfites. By virtue of increased CBS activity, these sulfur groups that were complexed as part of The Methylation Cycle can now be released into the system as sulfites which are toxic to the body and put an additional burden on the SUOX gene product. This creates a greater need for both molybdenum and B12. In addition, the presence of yeast in the gut may exacerbate the need for molybdenum.

When molybdenum levels drop particularly low, I find that we start to see boron and vanadium dumping on Hair Elements tests, in these cases I suggest a UAA to check that taurine levels are not too high. We need sufficient molybdenum to process excess taurine and that may be an issue if molybdenum is too low. Sensitivity to sulfur products and sulfur containing antibiotics is often symptomatic of these CBS SNPs. High level excretion of thorium on a Hair Elements test may also be an indicator that taurine is higher than ideal and would be another reason to run a UAA to check taurine levels and consider that CBS may be out of balance.

Those who are CBS + may tend toward excessively high taurine levels on a urine amino acid (UAA) test once Methylation Support is in place. Until adequate support for The Methylation Cycle is in place the impact of the CBS SNP is often not seen. I have previously used the analogy of a leaky bathtub to illustrate the impact of a CBS SNP with increased activity. If you think of the CBS SNPs as a leaky plug in a bath tub you can understand that until you fill the tub with water you cannot tell that the drain plug isn't sealing properly and is causing the tub water to flow down the drain instead of filling the tub. In a similar fashion, you cannot see the impact of the CBS SNP until you have sufficient Methylation Support in place such that the cycle is filling and at that point the taurine levels will rise well above the 50th percentile on a UAA if CBS is functioning at an increased level. Work with your health care professional to use follow up UAA testing to monitor taurine levels and supplementation along with regular UAA testing for taurine levels. In addition, non ideal gut microbes can cause an increase in CBS activity. Gut inflammation leads to an increase in TNF alpha, which in turn has been shown to increase CBS.

Oxidative stress has also been shown to increase CBS activity (Niu et al 2015). SAMe supplementation can also increase CBS activity. Thus, the combination of a CBS SNP that increases activity combined with non ideal gut bugs and a need for SAMe can necessitate close monitoring of taurine on a UAA as a means to follow excessive CBS activity. While limiting SAMe is not an answer for those who are AHCY + or COMT - -/Taq + +, it does mean an extra need to really keep those gut bugs in balance for those who need to be using extra SAMe.

The level of cysteine helps to determine if glutathione or taurine is produced from the transulfuration reaction. High levels of cysteine favor the conversion of cysteine to sulfate and taurine rather than to glutathione. Consequently, the elevated rate of conversion of homocysteine to cysteine due to increased CBS activity would result in the subsequent conversion of cysteine to taurine and sulfate rather than to glutathione.

I focus on those CBS SNPs that lead to increased CBS activity and literature supports the finding that these are upregulations in the CBS enzyme (Hum Mutat. 2007 Sep;28(9):856-65., Clin Genet. 2000 Dec;58(6):455-9., Mol Genet Metab. 2000 May;70(1):53-60. Ann Hum Genet. 1998 Nov; 62(Pt 6):481-90. Hum Mol Genet. 2001 Mar 15;10(6):635-43. Mol Genet Metab. 2004 Mar;81(3):209-15).

There are also mutations that lead to decreased CBS activity. The SNP panel I designed does not test for those. However, the SAMe/ Homocysteine test (suggested above for AHCY +) should be a good indicator for a lack of CBS activity. In addition, in cases of high homocysteine and low taurine extra SAMe (as tolerated) along with Ultimate B Complex and extra magnesium can be considered.

Key Supplements to Consider for CBS A360A + - or + + | C699T + - or + + | N212N + - or + +

- Molybdenum cap and/or Molybdenum drops
- Black Bear Spray
- Extra Phosphatidyl Serine Complex
- to help with the stress/fight or flight response

- DHA
- Low dose lithium and potassium based on HE test results
- Extra hydroxy B12 and adenosyl B12 and methyl B12 (as tolerated) c
- Attention nucleotide blend due to fight or flight response
- Intact Multigland to help with the stress/fight or flight response
- Stress nucleotide blend to help with the stress/fight or flight response
- Ora-Adrenal to help with the stress/fight or flight response
- CBS + nucleotide blend (check taurine levels after 4 to 6 weeks of support)
- Ultifend to aid with oxidative stress
- Basic Methylation Support

Biochemical Tests to Assess Progress for CBS A360A + - or + + | C699T + - or + + | N212N + - or + +

- Hair Elements (HE) test to check for lithium, molybdenum, boron, vanadium
- GI 360 test for non- ideal gut bugs that can increase CBS activity
- Urine Amino Acids test (UAA) on a regular basis to check taurine levels
- Comprehensive Neurotransmitter test (NC) to check epinephrine and norepinephrine levels for attention issues

SNP Results	Supports to Consider	Personalized Shopping List
CBS A360A + - or + + C699T + - or + + N212N + - or + +	Molybdenum capsules	☐
	Molybdenum drops	☐
	Black Bear Energy spray	☐
	Phosphatidyl Serine Complex softgels	☐
	DHA softgels	☐
	Lithium Orotate capsules	☐
	Lithium Drops	☐
	Potassium drops	☐
	Potassium capsules	☐
	Hydroxy B12 MegaDrops	☐
	Adenosyl B12 MegaDrops	☐
	Methyl B12 MegaDrops	☐
	Intact Multigland capsules	☐
	Ultifend capsules	☐
	Ora-Adrenal capsules	☐
	Stress Foundation nucleotide blend	☐
	CBS + nucleotide blend	☐
	Attention Support nucleotide blend	☐

	Basic Methylation Support	☐

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COMT V158M - -

If an individual has a COMT variation it means that they have a change in one of the amino acids of the enzyme. In the case of COMT one of the frequent amino acid changes is from a valine to a methionine. This is what is being tested for when the COMT V158M SNP test is run. The lab is able to look at the DNA to determine the information for which of these two amino acids that your copy of COMT contains. If you are COMT- it means that you do not have methionine in that spot of the enzyme and you have valine there instead. Having a valine in that spot is considered the "norm" and is a more efficient form of the enzyme. An individual who is COMT- (with the valine in that spot) will break dopamine down more efficiently.

The COMT enzyme uses methyl groups to help to inactivate dopamine. "COMT" stands for catechol-O-methyltransferase. So that when the COMT is working to inactivate dopamine and norepinephrine it does so by using methyl groups that you have available in your system. These methyl groups are donated by SAMe that is generated via the methylation pathway. Individuals who have the more efficient form of COMT may tend to use more methyl groups because they are inactivating dopamine more efficiently. Thus a COMT - - individual may need additional support for methyl groups for other reactions in the body.

I have found that both the COMT status, as well as the VDR Taq genes act in concert to have an impact upon overall need for methyl donors and dopamine support. In general, individuals who are COMT - - will have more consistent steady yet lower levels of dopamine due to enhanced COMT activity and will need and are able to tolerate higher doses of methyl donors.

In addition to COMT, two of the three vitamin D receptor SNPs also appear to play a role in dopamine levels and methyl donor tolerance. I believe that this is due to the relationship between vitamin D receptor and dopamine levels. Vitamin D increases the level of the enzyme involved in synthesizing dopamine. Increased levels of vitamin D would be expected to lead to increases in dopamine, norepinephrine and epinephrine. The VDR/Taq - - genetic status results in higher levels of vitamin D. Therefore, individuals who are negative for the VDR Taq polymorphisms (VDR /Taq - -) may have higher levels of dopamine due to enhanced levels of vitamin D. As would be expected if this were the case, I have found that these individuals are more sensitive to nutritional supplementation with methyl donors and nutrients that enhance dopamine levels than individuals who are homozygous (have both copies) for the VDR/Taq + + variation.

A primary function of this gene is to help to break down dopamine. Dopamine is a neurotransmitter that is recognized for its role in attention, as well as reward seeking behavior. Dopamine helps to cause pleasurable feelings that aid in reinforcing positive behaviors and motivating individuals to function in certain reward gaining activities. COMT is also involved in the breakdown of another neurotransmitter, norepinephrine. The balance between norepinephrine levels and dopamine levels has been implicated in ADD/ADHD; in addition, dopamine levels are important in conditions such as Parkinson's disease.

COMT is also involved in the proper processing of estrogen in the body. Females who are COMT - - may have less of an issue with excess estrogen building in their systems. Regardless, the use of indole 3 carbinol, broccoli extracts, calcium glucarate can be considered if excess estrogen is an issue.

Sensitivity to pain has recently been found to be correlated with COMT activity, such that COMT - - individuals have been shown to have a higher tolerance to pain.

Key Supplements to Consider for COMT V158M - -

- Extra SAMe
- Extra methyl B12
- Methyl MAX
- <COMT - - nucleotide blend
- Basic Methylation Support

Biochemical Tests to Assess Progress for COMT V158M - -

- Hair Elements (HE) test to check for lithium and arsenic
- Urine Amino Acids test (UAA) to check taurine levels relative to methionine as a measure of The Methylation Cycle
- Organix Comprehensive Profile test (OAT) to check FIGLU as a measure of The Methylation Cycle

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SNP Results	Supports to Consider	Personalized Shopping List
COMT V158M - -	SAMe tablets	☐
	Methyl B12 MegaDrops	☐
	Methyl MAX capsules	☐
	COMT -/- nucleotide blend	☐
	Basic Methylation Support	☐

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MTHFR A1298C + - or + +

The MTHFR (methylenetetrahydrofolate reductase) gene product is at a critical point in The Methylation Cycle. It helps to pull homocysteine into the cycle, serving to aid in keeping the levels in a normal healthy range.

There are several SNPs in MTHFR that I look at: MTHFR C677T, MTHFR 3 and MTHFR A1298C. The first two, C677T and MTHFR 3 appear to impair the function of MTHFR in terms of its ability to function optimally in generating 5 methyl THF which is needed to react with homocysteine to produce methionine.

The third MTHFR SNP that we look at is different than the two described above. The A1298C mutation in the MTHFR enzyme represents an example of a variation in the regulatory region of an enzyme. The mutation in this case results in a change in the portion of the enzyme that binds to s-adenosyl-methionine (SAMe). The purported role of SAMe in binding to the MTHFR enzyme is to inhibit its reverse reaction or down regulate MTHFR in its role with respect to BH4. This A1298C mutation may then result in an enzyme that is insensitive to inactivation or down regulation by SAMe. This would fit with the data that has found that individuals with the A1298C mutation do not show increased levels of homocysteine. This is in contrast to individuals with the C677T mutation or the MTHFR 3 SNP that do show elevations in homocysteine levels. The A1298C mutation has been mapped to the SAMe regulatory region of the gene. Mutations in the A1298C do not lead to increased levels of homocysteine; as such until now it has been felt that this mutation may not be of serious consequence. Literature suggests that in addition to the forward reaction that leads to 5methyl THF, that the MTHFR enzyme can drive a reverse reaction leading to formation of BH4 from BH2. I believe that the A1289C mutation is associated with defect in this reverse reaction leading to the formation of BH4. If the reverse reaction is driven by SAMe binding to the regulatory site then the A1298C mutation would be associated with an inability to convert BH2 to BH4, and could result in exceedingly low BH4 levels.

This reaction, BH4 to BH2 is normally driven by the DHPR enzyme. However, this enzyme is inhibited by aluminum, mercury and lead. Toxic metal accumulation in the body is affected by the methylation pathway. As a consequence of impaired methylation cycle function, toxic metals can accumulate in the body that can decrease DHPR function and put more strain on the MTHFR driven pathway. If this hypothesis is correct, then individuals with MTHFR A1298C mutations could be seriously depleted in BH4. In addition, there are a number of specific mutations that impair the function of the DHPR enzyme.

Low levels of BH4 are associated with more severe parasitic infections, diabetes as well as hypertension and arteriosclerosis. Serotonin synthesis, dopamine synthesis as well as ammonia detoxification require BH4. Factors that lead to more ammonia, such as high protein diets, and CBS C699T mutations generate elevated levels of ammonia that needs to be detoxified. Each molecule of ammonia requires two molecules of BH4 for ideal detoxification. It is clear to see how several of these factors may act together to impact ammonia detoxification as well as optimal BH4 levels for neurotransmitter synthesis. Keeping ammonia levels under control is of paramount importance for overall health and wellness, especially for an individual with MTHFR A1298C or DHPR mutations, as any excess ammonia generated can drain limited stores of BH4. Reductions in the reserves of BH4 will impact upon serotonin levels and dopamine levels.

Key Supplements to Consider for MTHFR A1298C + - or + +

- Pteridin-4 and MTHFR Liver Caps
- MTHFR A1298C + nucleotide blend
- Low dose lithium and potassium based on Hair Elements (HE) test results
- Metal Away for A1298C as long as not pregnant or nursing
- Basic Methylation Support
- Full Methylation Support

Biochemical Tests to Assess Progress for MTHFR A1298C + - or + +

- Hair Elements (HE) test to check aluminum and other metals that can impair BH4 levels
- UTEE test to check aluminum and other metals that can impair BH4 levels
- FMT test to check aluminum and other metals that can impair BH4 levels
- Urine Amino Acids test (UAA) combined with Comprehensive Neurotransmitter test (NC) to be sure tryptophan and tyrosine

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are converting to serotonin and dopamine

- Neopterin/Biopterin test for A1298C to look at BH4 levels

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SNP Results	Supports to Consider	Personalized Shopping List
MTHFR A1298C + - or + +	MTHFR A1298C+ Liver Support capsules	☐
	Lithium Orotate capsules	☐
	Lithium Drops	☐
	Potassium drops	☐
	Potassium capsules	☐
	Pteridin-4 capsules	☐
	MTHFR A1298C + nucleotide blend	☐
	Basic Methylation Support	☐
	Metal Away capsules (as long as not pregnant or nursing)	☐
	Full Methylation Support	☐

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MTHFR C677T + - or + + | MTHFR 3 + - or + +

The MTHFR (methylenetetrahydrofolate reductase) gene product is at a critical point in The Methylation Cycle. It helps to pull homocysteine into the cycle, serving to aid in keeping the levels in a normal healthy range. Several mutations in the MTHFR gene have been well characterized as increasing the risk of heart disease, as well as cancer, and may play a role in miscarriages as well as other health conditions. In addition, my experience has been that often those who are C677T + + (and some who are C677T +) tend to have thicker, 'sticky' blood prior to supplementation to bypass this SNP. This may be related to a higher rate of miscarriages for some who are C677T +. Many on my protocol who are C677T + have had successful full term pregnancies after supporting The Methylation Cycle so it is functioning. As always you do want to work with your own health care professional and I am not a fan of starting a program once you are already pregnant. I believe in getting your body in balance prior to pregnancy as part of the preparation of a healthy full term delivery.

There are several SNPs in MTHFR that I look at: MTHFR C677T, MTHFR 3 and MTHFR A1298C. The first two, C677T and MTHFR 3 appear to impair the function of MTHFR in terms of its ability to function optimally in generating 5 methyl THF which is needed to react with homocysteine to produce methionine. C677T seems to be a less significant impairment of MTHFR function, whereas the MTHFR 3 SNP seems to have a more pronounced effect on the function of the enzyme. One way to infer the magnitude of the impact of a SNP on function is by looking at the presence of single (heterozygous) versus double (homozygous) SNPs in the population. I almost never see a MTHFR 3 + + status which I take as an indication of the severity of this particular genetic combination. While MTHFR C677T + + is not seen all the time, it is also not as rare as the MTHFR 3 + + status. In both the case of C677T + and 3 +, it is possible to supplement with the product that MTHFR should be generating when it functions optimally and that is 5 methyl THF. The use of 5 methyl THF will help bypass the issue of a less than optimal MTHFR C677T or MTHFR 3 situation. I have chosen to use only low dose 5 methyl THF in my general vitamin *All In One*, as the use of 5 methyl THF can trigger strong detox reactions in those who have had a lifetime with less than ideal levels of this compound in their systems. In addition, where the next steps in the pathway include combining 5 methyl THF with B12, I feel it is important to first be certain that lithium is in balance to assure B12 transport and also to be sure that the short cut/Basic methylation route has been supplemented. Even when I do add extra 5 methyl THF, I like to do so only with low dose support in a liquid format that can be dose controlled at a precise level. Many other programs and supplements containing 5 methyl THF do not do this. I personally feel that only moving slowly with 5 methyl THF and carefully controlling the dose is the responsible way to proceed with MTHFR C677T and MTHFR 3 + SNPs.

The reason for my concern about high dose 5 methyl THF is not limited to uncomfortable levels of detox. Again, it is important to consider the entire methylation pathway and not just look at the impact of a single SNP or the advantage of a single supplement. When excess plain folate is present it can break down into glutamate. This is because folate is basically just a chain of glutamate molecules. Studies looking at the negative impact of high dose plain folate for certain SNPs would fit with this concern. While there are advantages of low dose plain folate, even for those with MTHFR SNPs (due to the effect of folate on other enzymes in this pathway), the use of high doses can be an issue. Once the 5 methyl THF that you have added to bypass the MTHFR SNP reacts with homocysteine to generate methionine it also generates THF. Like plain folate, THF contains glutamate residues. If there is also an SHMT SNP then it can function as a relief valve to allow the THF to be processed and dissipate. On the other hand, in the absence of an SHMT SNP or in the presence of high dose folinic then the use of high dose 5 methyl THF for those who are C677T + and MTHFR 3 + results in a buildup of components of The Methylation Cycle that can cause issues in the body.

This is an important point, so I am going to reiterate it another way. The concern is not just the need to bypass the MTHFR SNP by supplementing with 5 methyl THF. The other concern is the buildup of other forms of folate prior to the MTHFR step. Think of a bridge with a major accident on it so that traffic cannot get to the other side. The issue is not just getting to the other side so that you can continue on your journey (we are doing that by adding 5 methyl THF) BUT we also need to be concerned about the traffic jam prior to the bridge. All of those cars that are stuck there and do not have a way off the entry road to the bridge. Because the highway loops around all of the cars that are able to bypass the crash by entering the highway just past the bridge are going to eventually end up stacked behind the cars that are already there waiting for the accident to clear. This is why I do not want you to add high dose 5 methyl THF, and only to use low dose 5 methyl THF as needed to allow the critical homocysteine to methionine conversion to occur. This is also why I do not want you to add high dose folinic as that will block the relief valve that lets cars off the road instead of circling around until they are stacked behind all of the other cars. This is why you want to think about the entire pathway as a whole, not just look at what is needed to bypass a single SNP as they do not exist in isolation of each other.

The C677 and MTHFR 3 mutations in the MTHFR gene impact the ability of the body to convert homocysteine to methionine. MTHFR C677T and 3 SNPs in the MTHFR gene will therefore lead to increased levels of homocysteine if the body is not supplemented

properly to address this mutation. High levels of homocysteine have been mentioned in association with heart disease, Alzheimer's disease, as well as a range of inflammatory conditions. What this means is that individuals with the MTHFR C677T and MTHFR 3 SNPs are less able to make 5 methyl tetrahydrofolate and require supplementation with this form of folate to bypass this mutation.

Key Supplements to Consider for MTHFR C677T + - or + + | MTHFR 3 + - or + +

- Low dose additional liquid Methyl Folate MegaDrops for C677T and MTHFR 3
- Extra Phosphatidyl Serine Complex
- MTHFR C677T + nucleotide blend
- MTHFR 3 + nucleotide blend
- Heart Support nucleotide blend for older adults
- Basic Methylation Support
- Full Methylation Support

Biochemical Tests to Assess Progress for MTHFR C677T + - or + + | MTHFR 3 + - or + +

- Hair Elements (HE) test to check lithium for C677T and MTHFR 3 as you want to be sure you can progress to Full Methylation due to the need for low dose 5 methyl folate
- Organix Comprehensive Profile test (OAT) for C677T and MTHFR 3 to check FIGLU as a measure of progress with methylation
- Urine Amino Acids test (UAA) and/or SAMe/Homocysteine test for C677T and MTHFR 3 to be sure homocysteine levels are not too high

SNP Results	Supports to Consider	Personalized Shopping List
MTHFR C677T+ - or + + MTHFR 3 + - or + +	Methyl Folate MegaDrops	☐
	Phosphatidyl Serine Complex softgels	☐
	MTHFR C677T + nucleotide blend	☐
	MTHFR 3 + nucleotide blend	☐
	Heart Support nucleotide blend	☐
	Basic Methylation Support	☐
	Full Methylation Support	☐

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MTRR A66G + - or + + | MTRR S257T + - or + + | MTRR K350A + - or + + | MTRR R415T + - or + + | MTRR H595Y + - or + + | MTR A2756G + - or + +

MTR and MTRR are the abbreviations for *methionine synthase and methionine synthase reductase*.

These two gene products work together to regenerate and utilize B12 for the critical "long way" (AKA Full Methylation) around The Methylation Cycle, helping to convert homocysteine to methionine. High levels of homocysteine have been implicated as risk factors in a number of health conditions including heart disease as well as Alzheimer's disease. As is the case for COMT and VDR Bsm/Taq, the MTR and MTRR composite status is also important. Mutations in MTR have been reported to increase the activity of this gene product so that it leads to a greater need for B12 as the enzyme is using up B12 at a faster rate.

Those who are MTR + should consider closely monitoring lithium levels and should work to ensure that the 'short cut' (Basic Methylation) is firmly in place along with working on the 'long route' (Full Methylation) while routinely checking that lithium stays in balance.

Methionine synthase reductase (MTRR) acts in concert with methionine synthase (MTR) enzyme to recycle homocysteine back to methionine. The function of methionine synthase reductase (MTRR) is to regenerate methyl B12 for methionine synthase (MTR) to utilize. Mutations that impair the function of MTRR will have secondary consequences on the activity of the methionine synthase gene. Even if there are no mutations in the methionine synthase gene, the inability of MTRR to regenerate sufficient methyl B12 will impact upon MTR activity in The Methylation Cycle.

The combination of a mutation in MTRR that compromises its ability to regenerate B12, in concert with a MTR upregulation that is utilizing B12 at an accelerated rate would result in severely depleted levels of methyl B12 in the body. This would also create a roadblock in the methylation pathway between methionine and homocysteine that would require nutritional bypass for restored pathway function.

Because lithium helps to transport B12, when B12 is being utilized at a faster rate it can also lead to a depletion of lithium. I believe this is why I characteristically see an initial pattern of high level lithium excretion for those who are MTR + followed by depletion of lithium to the point where there is no detectable lithium on either hair or blood tests. Work with your own health care professional to support lithium with nutritional sources such as Lithium Drops, Lithium Orotate, BeCalm Spray, Bio-Nativus minerals. In addition, extra potassium and CoQ10 should always be used along with lithium support. After several months of lithium support I like to also check that iodine is in balance as iodine and lithium may compete with each other for entry into the cell.

Until you are certain that lithium is in balance I highly suggest only focusing on the Short Cut/Basic Methylation Support to support The Methylation Cycle. Adding extra B12 may serve to further deplete lithium until it is in balance. Those who are MTR + should run regular Hair tests or blood work to check lithium several times a year in my opinion. Where TMG can convert to DMG (and DMG shifts the balance toward the Long route/Full Methylation) this is again why I prefer the use of PS/PE/ PC and DHA to support the short cut/Basic Methylation rather than the use of TMG (or betaine). I feel that it is critical to truly have Basic Support in place first, while ascertaining that lithium is in balance before shifting to more focus on the long route/Full Methylation Support.

In terms of the MTRR SNPs, I find that simply MTRR A66G + is less of an issue when found as a single imbalance but MTRR A66G + + may have more significant impacts on the long route (Full Methylation). Homozygous (+ +) status is much less common for S257T, K350A, R415T and H595Y than MTRR A66G + +. This would suggest that these SNPs (S257T, K350A, R415T and H595Y) lead to a more serious impairment of MTRR function. My observation over time has been that SNPs that are not seen often, or SNPs that are never seen as + + (such as a true SUOX + +) or rarely seen as + + (such as S257T, K350A, R415T and H595Y) are ones that may cause more issues with methylation function.

Key Supplements to Consider for MTRR A66G, S257T, K350A, R415T, H595Y + - or + + | MTR A2756G + - or + +

- Extra Phosphatidyl Serine Complex
- Low dose lithium and potassium based on Hair Elements (HE) tests results
- MTR/MTRR caps
- MTR/MTRR nucleotide blend
- Extra B12 once lithium is in balance

- Basic Methylation Support
- Full Methylation Support

Biochemical Tests to Assess Progress for MTRR A66G, S257T, K350A, R415T, H595Y + - or + + | MTR A2756G + - or + +

- Hair Elements (HE) test to check lithium as you want to be sure it is in balance prior to progressing to Full Methylation
- Organix Comprehensive Profile test (OAT) to check FIGLU as a measure of progress with methylation
- Urine Amino Acids test (UAA) for to be sure homocysteine levels are not too high and to check methionine and taurine as measures of methylation function
- Urine Toxic & Essential Elements test (UTEE) to check for cobalt levels in urine once Full Methylation is in place
- Routine Urine Iodine test (UI) and HE tests to check iodine in urine and lithium in hair several times a year

SNP Results	Supports to Consider	Personalized Shopping List
MTRR A66G + - or + + MTRR S257T + - or + + MTRR K350A + - or + + MTRR R415T + - or + + MTRR H595Y + - or + + MTR A2756G + - or + +	MTR/MTRR/SUOX capsules	☐
	Hydroxy B12 MegaDrops	☐
	Adenosyl B12 MegaDrops	☐
	Get B12 spray	☐
	Black Bear Energy spray	☐
	Lithium Drops	☐
	Lithium Orotate capsules	☐
	Potassium drops	☐
	Potassium capsules	☐
	Phosphatidyl Serine Complex softgels	☐
	MTR/MTRR + nucleotide blend	☐
	Basic Methylation Support	☐
	Full Methylation Support	☐

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MTRR 11 + - or + +

While MTRR 11 is another SNP in the Methionine synthase reductase (MTRR) gene, the presence of this SNP seems to have a different impact than that of the MTRR SNPs described above. I have noted repeatedly over time that those who are MTRR 11 +, and especially those who are MTRR 11 + + tend to have issues with intestinal permeability and leaky gut. I often see high levels of mineral dumping on both Hair and urine mineral tests for those who are MTRR 11 + + . In addition, I often see high level amino acid dumping on UAA tests. When I talk about mineral and amino acid dumping in urine and hair, this is not a single mineral or amino acid I am talking about, it is more wide spread excretion of these nutrients. When you look at a HE test and a UAA and UTEE and see black lines across the page to the right on these tests think about checking MTRR 11 status.

Because of the excretion of nutrients, it is also a good idea to run a GI360 test to look for imbalances in gut microbes as leaky gut can be a factor with respect to gut bugs.

Key Supplements to Consider for MTRR 11 + - or + +

- AminoAssist for amino acid support
- Bio-Nativus minerals and Cell Food for mineral support
- VitaOrgan for general support for gut lining
- Leaky Gut nucleotide blend for general support for gut lining
- MTRR 11 + nucleotide blend
- Mitoforce and ATP to help support energy for nutrient transport
- Basic Methylation Support

Biochemical Tests to Assess Progress for MTRR 11 + - or + +

- Hair Elements (HE) test to check for overall mineral excretion
- Urine Toxic & Essential Elements test (UTEE) to check for overall mineral excretion
- Urine Amino Acids test (UAA) to check for overall amino acid excretion
- GI360 test to check for microbial imbalances
- Intestinal Permeability test (IP) to check for intestinal permeability

SNP Results	Supports to Consider	Personalized Shopping List
MTRR 11 + - or + +	AminoAssist capsules	☐
	AminoAssist spray	☐
	Bio-Nativus Mineral Drop Complex	☐
	Cell Food drops	☐
	VitaOrgan capsules	☐
	Mitoforce capsules	☐
	ATP tablets	☐
	Leaky Gut nucleotide blend	☐
	MTRR 11 + nucleotide blend	☐
	Basic Methylation Support	☐

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SHMT C1420T + - or + +

The SHMT gene product (serine hydroxymethyltransferase) helps to shift the emphasis of The Methylation Cycle toward the building blocks needed for new DNA synthesis and away from the processing of homocysteine to methionine. While DNA building blocks are important, mutations which affect the ability to regulate this gene product and interfere with the delicate balance of The Methylation Cycle may cause accumulations in homocysteine as well as imbalances in other intermediates in the body, as well as diverting and thus draining methylation cycle intermediates. The draining of methylation cycle intermediates, which appear to be critical for life and for health development, would fit with animal studies showing significant developmental issues with SHMT + status.

Where SHMT participates in several reactions, it is important to monitor a number of aspects of The Methylation Cycle to be sure all components are in balance. Looking at the ratio of thymidine to urine gives information about the nucleotide function of SHMT. Looking at the ratio of serine to glycine gives additional information about SHMT activity. Looking at homocysteine levels and glutamate levels along with FIGLU yields added data in terms of overall methylation cycle function and the impact of SHMT levels and support for SHMT.

Folinic acid limits SHMT activity, and iron increases its activity which is why I prefer only low levels of support, rather than high dose support for any methylation cycle compounds and I prefer to add supports individually based on each person's unique profile and their personalized biochemical data. Your SNP profile combined with your epigenetic profile creates a scenario for you that differs from others. A one size fits all supplement plan is not customized to your needs and could be detrimental to your needs. While it is more involved and time consuming, and yes, requires a greater understanding of these pathways, the need to adjust your supplement plan to suit your needs is what makes the most sense for better long term health in my opinion and experience. Your individualized supplement plan will likely change over time, as your biochemistry gets into better balance in spite of SNPs in your Methylation Cycle. This is why I emphasize looking at biochemical data, along with your SNP profile to personalize your supplement plan, and as always work with your own health care professional on final supplement decisions.

Key Supplements to Consider for SHMT C1420T + - or + +

- AHCY/SHMT caps
- Folinic + as needed
- Extra Lactoferrin as needed
- SHMT + nucleotide blend
- Naturomycin and Seasonal Support as needed for microbial imbalances
- Basic Methylation Support

Biochemical Tests to Assess Progress for SHMT C1420T + - or + +

- Hair Elements (HE) test to check for iron levels and lithium levels
- Urine Toxic & Essential Elements test (UTEE) to check for iron levels and cobalt levels
- Urine Amino Acids test (UAA) to check for methionine and taurine, glycine and serine to check methylation pathway
- Organix Comprehensive Profile test (OAT) to check for FIGLU as a means to check methylation pathway
- GI360 Test to check for microbial imbalances due to iron levels related to SHMT +

SNP Results	Supports to Consider	Personalized Shopping List
SHMT C1420T + - or + +	AHCY/SHMT capsules	☐
	Folinic + capsules	☐
	Lactoferrin capsules	☐
	Naturomycin capsules	☐
	Naturomycin spray	☐

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	Seasonal Support capsules	☐
	SHMT + nucleotide blend	☐
	Basic Methylation Support	☐

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VDR + - or + +

VDR is the abbreviation for *vitamin D receptor*. The panel I designed looks at more than one SNP of the vitamin D receptor, the Taq as well as the Fok sites. While the Fok change has been related to blood sugar regulation, changes at Taq can affect dopamine levels. For this reason it is important to look at the composite of the COMT and VDR/Taq status and make supplement suggestions based on the combined results at these two sites in terms of tolerance to methyl donors.

The focus on changes in the Fok portion of the VDR is in regards to supplements that support the pancreas and aid in keeping blood sugar in the normal healthy range. Understanding of the VDR SNPs is a bit more complicated; some researchers find health issues for FOK + and other describe health concerns for FOK -. This is why I believe the VDR/FOK cap is useful for all regardless of VDR FOK status.

In terms of Taq, those who are Taq - - tend to have less tolerance for methyl donors, those who are Taq + have more tolerance for methyl donors. So, an individual who is COMT + +/Taq - - would have the lowest level tolerance for methyl B12. The diametric opposite would be an individual who is COMT - -/Taq + + and would do well with higher amounts of methyl donors.

Key Supplements to Consider for VDR + - or + +

- VDR/Fok Cap
- Extra Vanadyl and Chromium as needed
- Glucose Support nucleotide blend as needed
- Bone Support nucleotide blend as needed
- Glucose Support cap as needed
- Vita D-Light spray as needed
- VDR/Fok + nucleotide blend
- VDR/Taq + nucleotide blend
- Basic Methylation Support

Biochemical Tests to Assess Progress for VDR + - or + +

- Hair Elements (HE) test to check for chromium and vanadium as they can impact blood sugar levels
- Urine Toxic & Essential Elements test (UTEE) to check for chromium and vanadium as they can impact blood sugar levels
- Cardiometabolic test if desired to look at markers for blood sugar imbalances
- Vitamin D test to directly measure vitamin D levels
- Bone Assessment test if desired as vitamin D can impact bone integrity

SNP Results	Supports to Consider	Personalized Shopping List
VDR + - or + +	VDR/Fok capsules	☐
	Vanadyl tablets	☐
	Chromium drops	☐
	Glucose Support capsules	☐
	Vita D-Light spray	☐
	Glucose Support nucleotide blend	☐
	VDR/Fok + nucleotide blend	☐
	Bone Support nucleotide blend	☐

	VDR Taq + nucleotide blend	☐
	Basic Methylation Support	☐

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Ion Transport & ACE

Two categories of DNA variations that are not currently measured on tests are what I call "Ion Transport" which includes minor changes in CFTR gene, as well as ACE (angiotensin converting enzyme) deletions. DNA SNP tests measure single base changes and both of these categories of variations include other types of changes to DNA including deletions and insertions. I do feel that it is important to consider support for these potential imbalances, especially as both may play important roles in mineral balance.

In a controlled study, I found that those with Autism consistently showed variations in the Ion Transport gene. When imbalances in Ion Transport are present, I often see particularly low potassium and lithium on Hair Elements tests. There can also be imbalances in chloride transport and this may impact gaba levels. Imbalances in Ion Transport may also play a role in apraxia/language development as well as issues with weight management. The use of the Ion Transport Support capsules and Ion Transport nucleotide blend are worth considering in these situations. It is important to note that Ion Transport supports can actually be considered by all regardless of low potassium levels however, the Ion Transport Support caps do include some low dose wasabi which can bind to mercury. As such, the use of wasabi may increase excretion of mercury. Due to this possibility, I therefore suggest that Ion Transport Support caps be used only as tolerated since some individuals have a difficult time with mercury excretion.

Similarly, issues with ACE can impact mineral balance. Changes can occur that affect the activity of the ACE gene that can lead to elevated blood pressure. In animal studies, imbalances in this pathway were also correlated with increased anxiety and decreases in learning and memory. Increased ACE activity can also throw off the essential mineral balance in your system due to decreased excretion of sodium in the urine and increased excretion of potassium in the urine. This reaction is also tied to the stress response, such that situations of chronic stress can result in additional sodium retention and increased potassium excretion which eventually can lead to potassium depletion. This excess potassium is excreted provided that the kidneys are functioning properly, in the event that kidney function is compromised, it can lead to the retention of potassium in the body.

Please Note: If you are on blood pressure medication, you will want to be particularly careful and as always consult with your health care professional when using any supplementation to support ACE imbalances.

Key Supplements to Consider for ACE & Ion Transport

- Ultra Dairy Digest
- Mitoforce
- L-carnitine
- Biotin
- Ultimate B Complex
- ACAT/BHMT cap
- Low dose lithium and potassium based on Hair Elements (HE) test results
- Ion Transport cap and nucleotide blend
- Ultifend
- Resveratrol spray
- CoQ10
- ACE + nucleotide blend
- Kidney Support nucleotide blend
- Kidney Beef capsules
- Basic Methylation Support

Biochemical Tests to Assess Progress for ACE & Ion Transport

- Hair Elements (HE) test to check for lithium, sodium and potassium levels
- Organix Comprehensive Profile test (OAT) to check lactate and pyruvate for conversion of food into energy cycle and check for ketones.
- Urine Amino Acids test (UAA) for high methionine
- Cardiometabolic test or alternative for cholesterol levels

- Blood pressure levels as monitored by your health care professional

SNP Results	Supports to Consider	Personalized Shopping List
ACE & Ion Transport	Ion Transport Support capsules	☐
	Mitoforce capsules	☐
	L-Carnitine tablets	☐
	Biotin capsules	☐
	Ultimate B Complex capsules	☐
	ACAT/BHMT capsules	☐
	Ultifend capsules	☐
	Resveratrol spray	☐
	Coenzyme Q10 spray	☐
	CoQ10 Enzyme softgels	☐
	Kidney Beef vegicaps	☐
	Ultra Dairy Digest capsules	☐
	Lithium Orotate capsules	☐
	Lithium Drops	☐
	Potassium drops	☐
	Potassium capsules	☐
	Ion Transport nucleotide blend	☐
	ACE + nucleotide blend	☐
	Kidney Support nucleotide blend	☐
	Basic Methylation Support	☐

SUBMIT YOUR SHOPPING LIST

By clicking “submit” you will receive a personalized list with each product that you selected within your MPA. This list will be uploaded to your Client Portal within your “Recent Documents” folder, you can then review it with your health care professional. Each product will include a hyperlink that (when clicked on) will forward you to the item of interest on www.HolisticHeal.com for your convenience.

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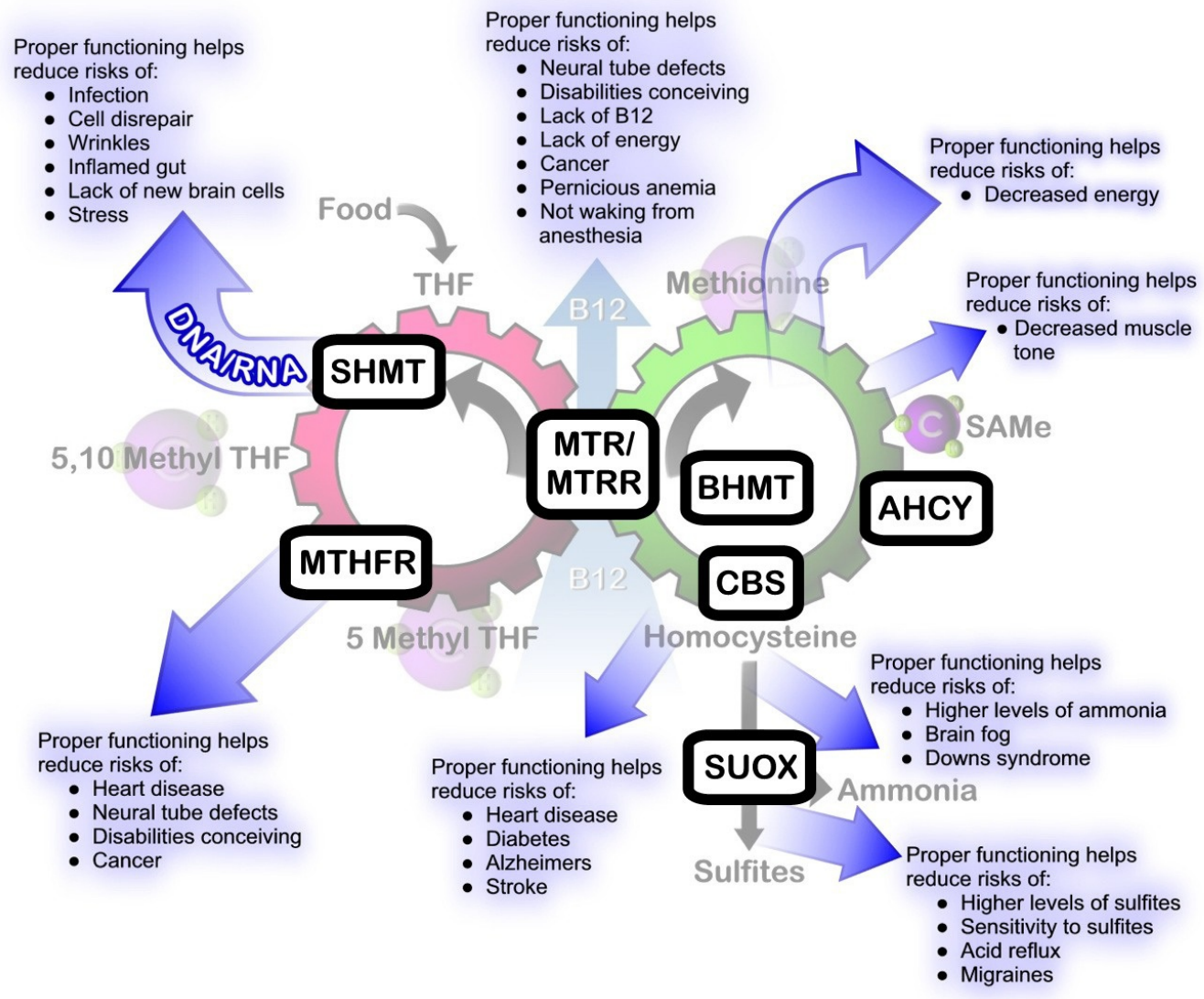
General Overview of Genes

The following diagrams illustrate the locations of the various SNPs within The Methylation Cycle. Specific information on each SNP noted for your personal SNP profile is compiled in this packet based on your customized results.



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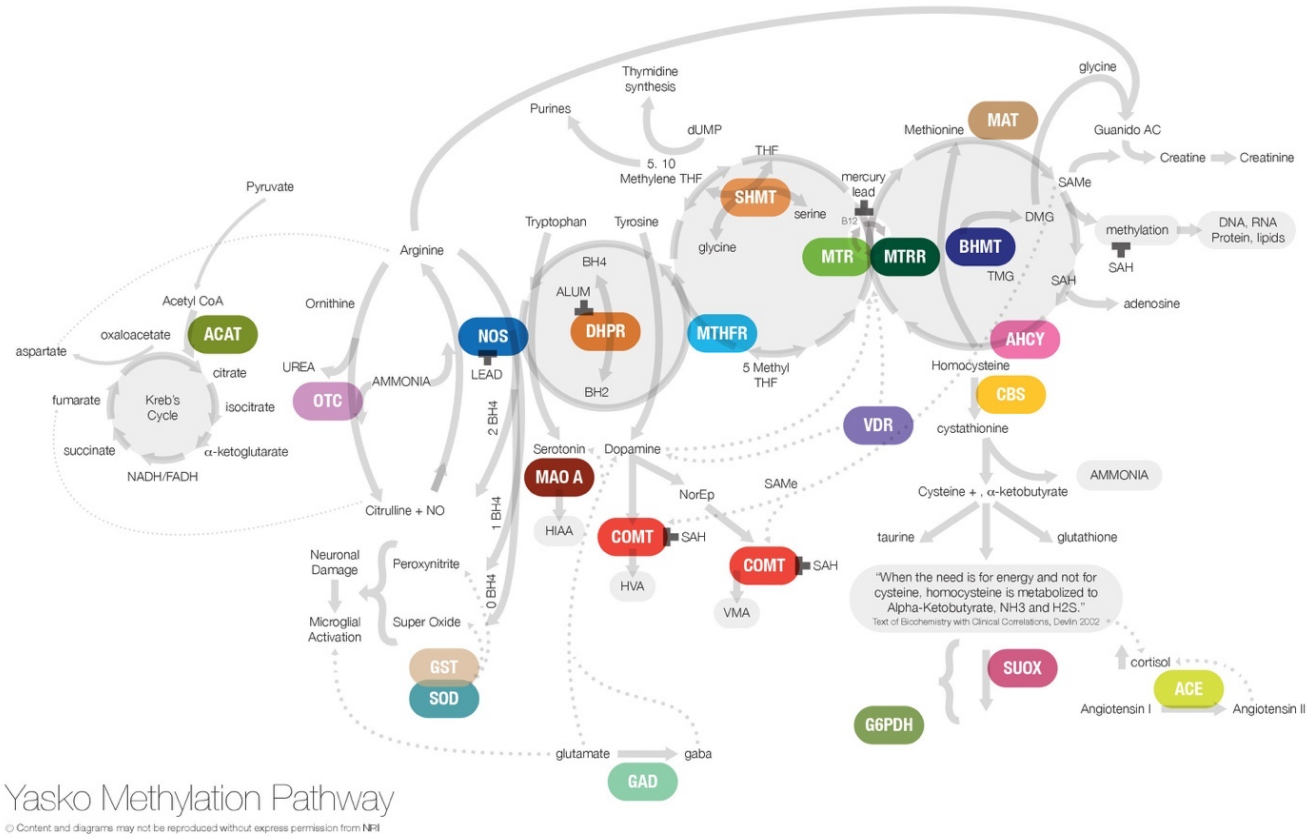

Yasko Methylation Pathway

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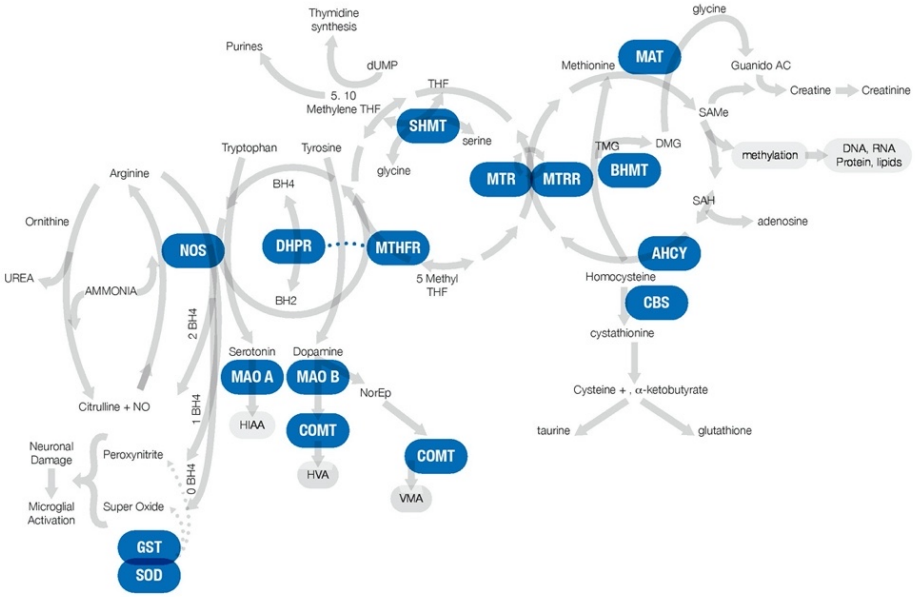
Yasko Methylation Pathway

1 The four cycles that make up the Methylation Cycle. This first diagram shows the pathways and the biochemical compounds that are a part of these cycles.

2 The second diagram layers on the location of the genes in the nutrigenomic test to show where the possible locations of SNPs are in these biochemical pathways. The location of the where these genes act on these pathways are in color.



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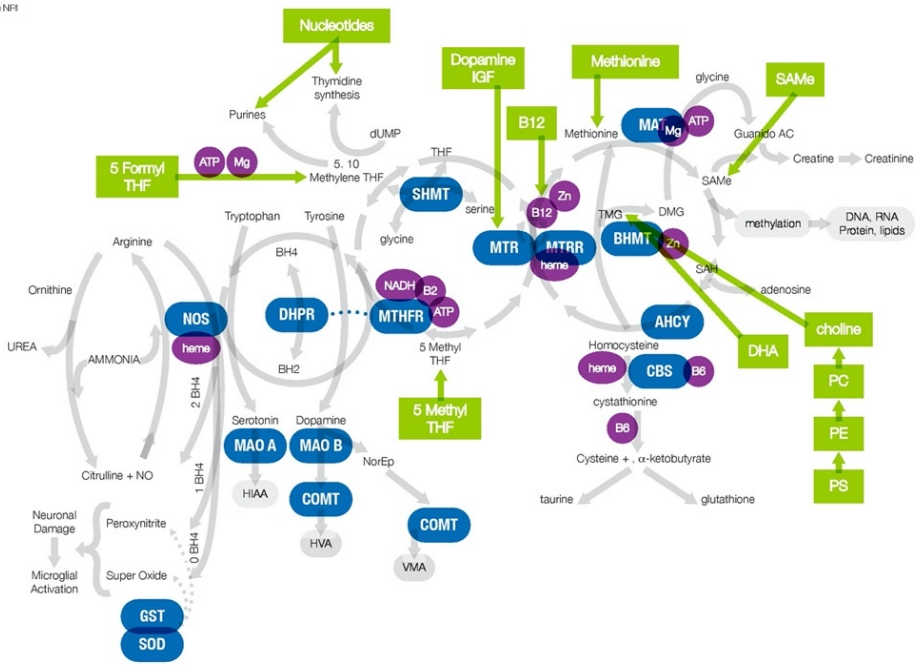
2. The second diagram layers on the location of the genes in the nutrigenomic test to show where the possible locations of SNPs are in these biochemical pathways. The location of the where these genes act on these pathways are in color.
3. The products of the genes often require what are called "cofactors" which are helpers that aid the gene in their function. The cofactors are noted in purple circles.
4. There are places where nutritional support can be added to feed into these pathways. This helps to get around blocks due to malfunctions in the blue boxed genes. The places and names of the supplements that can be added to bypass mutations and where they can feed in to help with these pathways are in green.



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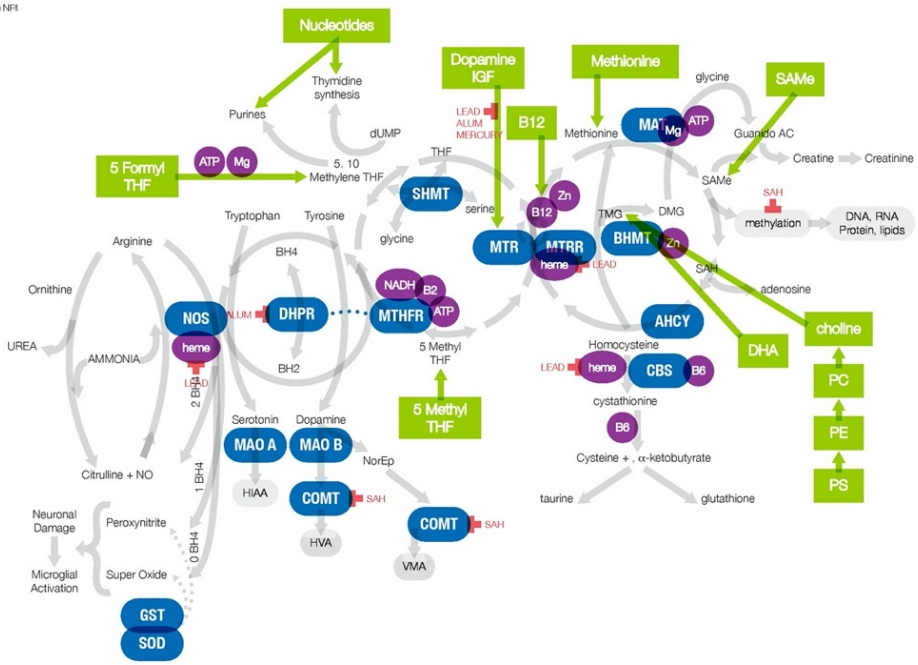
5. Toxic metals can inhibit steps in these pathways even if there are not blocks due to mutations. Also products from the pathway can inhibit other reactions in the pathway. The locations of where the pathways are inhibited are noted in red.



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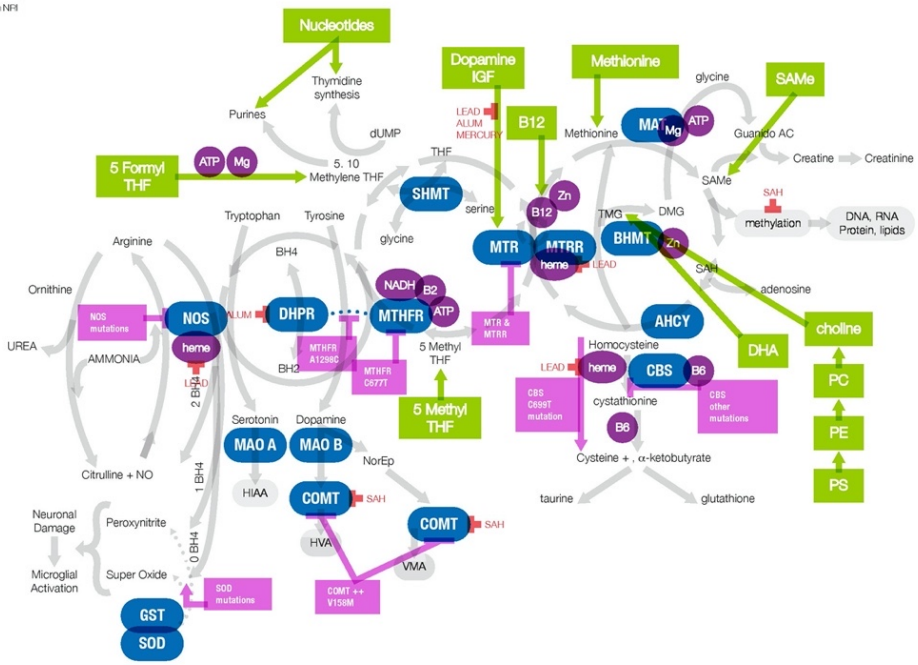
6 The actual SNPs, or mutations in the genes are noted in pink. Recall that the genes in this pathway that are looked at by nutrigenomic testing are in blue boxes. The pink boxes show where the mutations in these genes occur thus affecting the position in the cycle where they are located.



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